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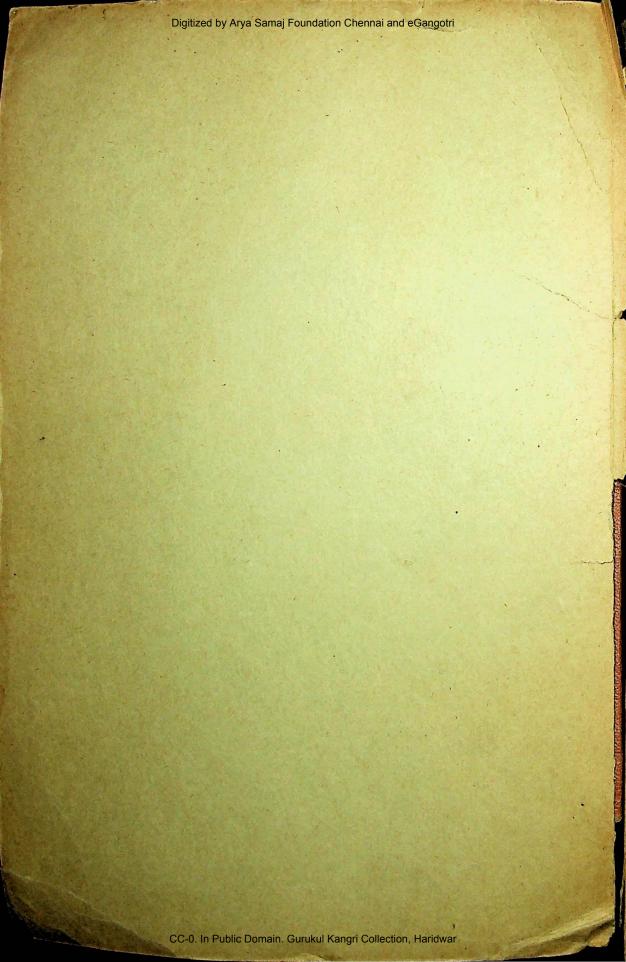
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VOLUME IX

XXV INTERNATIONAL CONGRESS
MUNICH, 1971

ABSTRACTS OF VOLUNTEER PAPERS
AND FILMS





XXV INTERNATIONAL CONGRESS OF PHYSIOLOGICAL SCIENCES

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ABSTRACTS OF VOLUNTEER PAPERS AND FILMS



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Supplement

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Volume II

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Volume III

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EFFECT OF MORADRENALINE ON ACTIVITY IN SINGLE AORTIC BARORECEPTOR FIBRES. H. Aars. Inst. Exper. Med. Res., Univ. of Oslo, Ullevaal Hosp., Oslo, Norway.

The possibility that the sympathetic nervous system may be able to control the sensitivity of arterial baroreceptors has been examined in the present study by recording single fibre activity in the left aortic nerve of rabbits before and during intravenous infusion of 4-6 µg/kg·min of noradrenaline. Activity was related to blood pressure, which could be changed by bleeding and re-infusion of blood, and to diameter of ascending aorta measured with ultrasonic technique inside the intact thorax. At equal blood pressures, activity of 34 single, medium-sized and thick medullated fibres was slightly lowered by noradrenaline, on average by 1 spike/pulse beat. At the same time, diastolic aortic diameter was reduced by about 7%. However, when compared at equal diastolic diameters, receptor activity was found to be increased by noradrenaline by 2-3 spikes/pulse beat, or up to 50%. Some of the thin medullated fibres, with conduction velocities of about 5 m/sec, showed a rise of activity even at comparable blood pressures. The results indicate that sympathetic control of aortic baroreceptors can be effected by regulation of smooth muscle tone in the receptor area. Possibly due to different coupling of receptors in the aortic wall, the firing rate of the thin medullated fibres is increased more than that of thick and medium-sized fibres.

MYOCARDIAL CONTRACTILITY IN EXPERIMENTAL HEMORRHAGIC SHOCK. F.L. Abel. Dept. of Physiology and the Heart Research Center, Indiana Univ. Sch. of Med., Indianapolis, Ind. 46202, U.S.A.

Simultaneous measurements of left ventricular myocardial performance were made in dogs before, during, and after producing hemorrhagic shock by maintaining arterial pressure at 40 mm Hg for four hours. Afterload was controlled by a servo-controlled pump system while simultaneous recordings were made of stroke volume, peak power, stroke work, dp/dt, df/dt, end diastolic pressure, and left atrial pressure. Ventricular function curves were produced by altering left atrial pressure via an arterial to atrial shunt. After reinfusion the curves obtained were essentially identical to those prior to hemorrhage. Despite the open-chest preparation, no evidence of ventricular failure was seen until long after the arterial pressure decreased in similar experiments in non-afterload controlled animals. These data are interpreted as indicating that the early decrease in cardiac output in the post-infusion period of experimental hemorrhagic shock in the dog is due to a decrease in venous return, secondary to increased capillary permeability to plasma proteins as demonstrated by the loss of radioactive iodinated serum albumin from the circulation. A decrease in myocardial performance occurs as a later phenomenon and contributes to the futher decline in cardiac output in the later part of the post-infusion period. (Supported by USPHS, NIH grants H6308 and HE10659.)

STEROIDS IN THE RAT AND FROG THYMUS! A.D.Abraham, E.A.Pora and N.Sildan. Department of Animal Physiology, University of Cluj, Romania

Rat and frog thymi contain steroid substances: intermediate products of cholesterol biosynthesis, cholesterol and cholesterol-like steroids. (1-¹⁴C)acetate and (4-¹⁴C)cholesterol in vitro could be converted into ¹⁴C labelled steroids of thymi. Some steroids were identified by thin layer and column chromatography and UV and IR spectrophotometry.

Rat thymus steroid spectrum is very similar with the frog thymus spectrum; between these there are only quantitative differences. Changes of steroid contents of both thymi depending on the sex, age and other physiological conditions were observed.

4 EFFECT OF ESTROGEN ON VAGINAL BLOOD FLOW IN NONPREGNANT EWES. R. M. Abrams, D. Caton and J. A. J. Stolwijk, Department of Obstetrics and Gynecology, University of Florida College of Medicine, Gainesville, Florida and John B. Pierce Foundation, New Haven, Connecticut.

The temperature of the uterus of anestrous or ovariectomized ewes is normally 0.2 - 0.4°C higher than the temperature of the aortic blood. Two hours after an injection of 0.5 - 1.0mg estrone this temperature difference is nearly abolished (<0.05°C) because of a marked increase in blood flow, and thus, heat loss from the uterus. A similar thermal response occurs between other parts of the reproductive tract and the aorta. Also, the temperature difference between the deep and the more peripheral, cooler tissues of the vagina is significantly diminished after estrone injection. The vaginal hyperemia induced by estrogens has been measured more directly with a self-retaining vaginal heat flow device containing four heat flow discs. Tap water circulating through the probe provided the heat sink. Thermal conductances in four anestrous ewes were 0.085 ± 0.003(S.D.) cal·cm⁻² surface of probe·min⁻¹·°C⁻¹. Three hours after an injection of lmg estrone i.m. the conductance had risen to 0.102 ± 0.077(S.D.) cal·cm⁻² surface of probe·min⁻¹·°C⁻¹. The timing of the response was similar to that of uterine hyperemia as judged by the decrease in temperature difference between uterine cavity and aorta.

5 EXTENT OF AREA IN MOTORSENSORY CORTEX OF THE CAT WHERE MICROSTIMULATION ACTIVATES A SINGLE ALPHA MOTONEURON.
Physiology, New York Medical College, New York, N.Y., U.S.A.

The technique of intracortical microstimulation was used to determine the size of the cortical zone which activates a single alpha motoneuron (AMN). A train of eleven 200-µsec stimulus pulses was applied every two seconds through a tungsten microelectrode, and the response of AMNs serving distal muscles of the contralateral forelimb was determined by recording motor unit potentials with bipolar EMG electrodes. When motor unit activity was recorded in response to intracortical microstimulation, the stimulating microelectrode was moved to determine the length along the track where stimulation was effective for each recognizable unit. During microelectrode advancement the stimulating current was kept constant at 20 µamp or less. It was found that the zone of cortex from which a single AMN could be activated by such small stimulating currents was restricted. Out of sixteen AMNs fourteen could be activated from only one cortical point or from two points located 100 microns apart.

(Supported by Pre-Doctoral Fellowship No. GM-33,978 from NIH.)

6 BINDING OF CORTICOSTEROIDS TO TARGET ORGANS. Zs.Ács and E.Stark Department of Pathophysiology, Institute of Experimental Medicine Hungarian Academy of Sciences, Budapest, Hungary.

It is now widely belived that for its effect a hormone depends on its being bound to a target. The binding of corticosterone to rat liver slices was studied by the displaceable binding method. The findings point to the existence of at least two types of sites differing in the number of surfaces and in their association konstants. To produce a lasting corticosterone deficiency bilateral adrenalectomy was performed: 14 days later the number of the binding surfaces was found to have increased in both types. In rat kidney slices attemts to demonstrate a binding site were unsuccessful, nor did the liver slices bind the biologically inactive tetrahydrocorticosterone. It is concluded that biological action, and perhaps metabolism of corticosteroids depend on their being bound to the target organ.

POSTERIOR HYPOTHALAMIC THERMAL STIMULATION CAN ALTER BEHAVIORAL, BUT NOT PHYSIOLOGICAL, TEMPERATURE REGULATION. Eleanor R. Adair and J. D. Hardy. John B. Pierce Fndn. Lab., New Haven, Connecticut, U.S.A.

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Thermode and thermocouple re-entrant tubes were implanted unilaterally in both medial preoptic area (A13.0,L0.5,D+1.0) and the posterior hypothalamus (A7.5,L1.5,D+1.5) of one squirrel monkey. Water perfusion of the thermodes adjusted preoptic and/or posterior hypothalamic temperature between 35 and 43°C. Preoptic, posterior hypothalamic, rectal, ambient, and four skin temperatures were monitored during behavioral temperature regulation. The animal's chamber was heated and cooled by forced convection. The monkey controlled the air temperature by selecting between two preset air source temperatures, 10 and 50°C. When either preoptic temperature or posterior hypothalamic temperature was changed, the monkey changed the air temperature in the opposite direction by a proportional amount. Skin and rectal temperatures shifted in the same direction as the environment. The results appeared identical for equivalent thermal stimulation of either area. In a neutral environment (33°C), with behavior absent, changes in preoptic temperature alone stimulated physiological mechanisms of heat gain or heat loss, but changes in posterior hypothalamic temperature, keeping preoptic temperature constant, did not.

ON THE MECHANISM OF CONDITIONAL EVOKED POTENTIALS. G. Adam. Dept. of Comparative Physiology, Ectvos Lorand University, Budapest, Hungary.

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Conditional evoked potentials /CEP/ have been elaborated by the delayed pairing of splanchnic and sciatic electrical shocks in order to follow up some basic mechanisms of this form of elementary learning. After the appearance of the CEP complete reversible cessation of the cerebral electrical activity for a period of 1-4 minutes has been obtained by means of cooling and/or total "stop-flow" of the brain circulation. After the restitution of the normal ELG-pattern the CEP persisted, moreover, the amplitude of the conditional deflections increased in most cases. Evidence is presented supporting the role of synaptic depletion-mechanisms and denying the reverberatory nature of this form of memory-storage.

IDENTIFICATION OF INVERTEBRATE CARBONIC ANHYDRASE. A.D.F. Addink. Laboratory of Chemical Animal Physiology, University of Utrecht, The Netherlands.

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The blood of Mollusca and Crustacea does not contain any carbonic anhydrase activity. This enzyme involved in acid-base regulation and CO2-transport is located in tissues, e.g. mantle muscle or gill of Sepia officinalis. An isolation procedure based on solubilization with detergents and salting out will be presented (45 x purification). The invertebrate enzyme activity is completely dependent on tightly bound zinc, as has been determined by chelation with 1,10-ortho-phenanthroline. The invertebrate enzyme is found to be comparable to the human erythrocyte carbonic anhydrase isoenzyme type C and bovine erythrocyte carbonic anhydrase isoenzyme type B with respect to hydration kinetics (stopped-flow measurements), electrophoretic mobility, the essential role of zinc and the inhibition by sulfonamides.

10 RECORDING OPTIC NERVE ACTIVITY UNDERWATER FROM A FREELY-MOVING HORSESHOE CRAB. A.R.Adolph Neurophysiology Laboratory, Retina Foundation, Boston, Mass. U.S.A.

A new technique has been developed for long-term, extracellular, multi-fiber recording from intact optic nerve in a freely-moving animal. Using this technique, lateral eye nerve activity has been recorded from animals underwater, with minimal restraint from a flexible, neutrally-buoyant, signal cable. The experimenter, using SCUBA equipment and carrying the recording electronics in a water-tight housing, accompanied the animal underwater. Coded tone signals, corresponding to a repertoire of simple behavioral patterns during optic nerve activity, were also recorded. The experimental techniques and field operations, including some underwater photographs, are illustrated and described. Some temporal patterning of spikes can be seen within the continuous, fluctuating background of optic nerve activity occurring in a natural underwater environment. Ancillary observations were also made of underwater behavior by untethered, non-implanted animals.

CONDITIONING OF SINGLE UNITS IN THE LATERAL GENICULATE OF CAT. C. Adorjani, R. von der Heydt, H.M. Keller, and G. Baumgartner. Dept. of Neurology, Univ. of Zürich, Switzerland.

We investigated the problem whether neuronal mechanisms of learning exist in modality-specific nuclei. The activity of single units in the LGB of acute cat preparations was recorded during conditioning experiments. Spike discharges were averaged as Post Stimulus Time Histograms (PSTH). Responses of units with peripheral receptive fields of more than I degree arc were phasic or phasic-tonic, and could be influenced by conditioning procedures. Following the conditioning, four different phenomena were observed in the PSTHs: (1) long-lasting (up to 20 min) change of latency of the primary component; (2) short-lasting (several sec) amplitude change of selective components; (3) short-lasting persistence of consolidated discharge rhythms; (4) long-lasting amplitude change of selective components, e.g. activity rebound at the latency of the former UCS. All on-center units and most off-center units showed effects (1) and (2); some off-center units showed effects (3) and (4). Units with receptive fields of less than 1 degree arc near the fovea exhibited tonic responses which could not be influenced by long-lasting conditioning procedures. - The results indicate that certain single units in the LGB participate in basic learning stages.

FUNCTIONAL RELATIONSHIP BETWEEN NEOCORTEX AND PALEOCORTEX IN THE SOUTH AMERICAN ARMADILLO CHAETOPHRACTUS VILLOSUS. J.M. Affanni, L. Garcia Samartino. Chair of Physiology, University of Buenos Aires, Buenos Aires, Argentine.

Because of its neuroanatomical features, we propose the South American armadillo Chaetophractus villosus as an excellent model for the study of the functional relationship between neocortex and paleocortex. The electrical activity and the chemical composition of paleocortex after total ablation of neocortex were described. The bioelectrical activity was studied in the states of wakefulness, "slow sleep" and "rapid sleep". Additional experiments were made in which the electrocortical activity and chemical composition of the neocortex were studied after ablation of large areas of paleocortex. The neocortical electrical activity after the above mentioned ablations was also studied during wakefulness, "slow sleep" and "rapid sleep". Special attention was given to the quantitative aspects of the total amounts of those three states both before and after the surgical and functional (spreading depression) ablations.

CHEST WALL SHAPE EFFECT ON PLEURAL SURFACE PRESSURE TOPOGRAPHY. E.Agostoni and E.D'Angelo. Inst. of Human Physiology, Univ. of Ferrara, Ferrara, Italy.

When the abdominal pressure in supine rabbits and dogs was decreased until the lung volume equalled that in the head-up posture at FRC, a cranio-caudal gradient of transpulmonary pressure similar to that in the head-up posture at FRC was produced. By further lowering the abdominal pressure the gradient became greater than that in the head-up posture at FRC. When the abdominal pressure in head-down rabbits was decreased until the lung volume equalled that in the head-up posture at FRC the vertical gradient was reversed and became nearly equal to that in the head-up posture at FRC. When the abdominal pressure in head-up rabbits was increased until the lung volume equalled that in the supine posture at FRC the vertical gradient was markedly reduced, when the abdominal pressure was further increased and the lung volume equalled that in the head-down posture at FRC the vertical gradient disappeared; it reversed only in exsanguinated rabbits. These results show that, except when the lung is engorged with blood, the distribution of transpulmonary pressure depends essentially upon the shape of the chest wall, which is mainly related to the gravity effect on its parts.

EFFECT OF SOME QUATERNARY AMMONIUM SALTS ON MEMBRANE POTENTIAL. St. Agrigoroaiei. Lab. of Animal Physiology. Center of biological research, Tassy, Romania.

The effect of some ammonium quaternary salts (tetra aethyl ammonium series) on single muscle fibre membrane potentials was studied in frog sartorius and long extensor muscle of the IV finger of the frog, using intracellular microelectrods. No depolarizing effect of any of the drugs was noted. Instead, a stabilizing effect could be demonstrated with all the compounds by the K depolarizing test. The magnitude of the effect was in proportion with the length of the alkyl groups. The stabilizing effect was greatly enhanced by replacing an alkyl by a phenyl group. By studying the phenomenon in time, it was noted that the evolution follows an exponential curve which had the tendancy to dwell at virtually constant values after approximately one hour's interval. The same values were found with both types of muscle fibres.

PHYSIOLOGICAL INVESTIGATIONS OF ULTRASONIC ECHO-LOCATION IN ANIMALS. E.Sh. Airapetjants and A.I. Konstantinov. Leningrad Univ. and the Pavlov Inst. of Physiology, USSR Acad. of Sci., Leningrad, USSR.

The knowledge of the mechanism and cerebral apparatuses of echo-location in animals widens the possibilities for a biological theory space analysis. At the XXIV-th Congress of Physiology the authors presented a report on some physiological characteristics of the echo-location system in bats. New evidence has been obtained which makes it possible to determine the physiological principles of ultrasonic location in two families of bats (Vespertilionidae and Rhinolophidae) and in Dolphins (Tursiops truncatus). On the basis of a number of indices it is possible to compare similar and specific properties of echo-location system in space analysis in the above mentioned animals. An evaluation of frequency and time characteristics of the auditory system of echo-locating animals, the level of the resolving power of natural locators for distance, the diapason of the echo-location discrimination of objects are given. The results of the investigation of the stages in the formation information in bats at different stages of postnatal development are presented.

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16 HIGHER NERVOUS ACTIVITY IN POSTNATAL ONTOGENESIS OF DOGS ANTENATALLY X-RAY IRRADIATED. M.G. Airapetyants. Inst. of Higher Nervous Activity and Neurophysiology, USSR Academy of Scieces, Moscow, USSR.

Higher nervous activity in postnatal ontogenesis was studied in dogs irradiated with a 200 r dose at different antenatal periods. Early irradiation uses subcortical structures. At later periods it provoked impairments of the cerebral cortex, but improvement was observed with age and complete recovery of the C.N.S. at the end of the Ist year of life. With early irradiation wave-like disturbances of higher nervous activity persisted. Tests revealed a latent functional deficiency of the C.N.S. Thus we dealt with two experimental models of brain pathology: with a predominant impairment of subcortical structures in one case and of the cerebral cortex in the other. The conclusion is drawn that the structural and functional disturbances of the cortex in antenatally irradiated dogs may be restored only with intact subcortical structures. Single doses of chlorpromasine (0,01 mg/kg) and seduxen (0,12 mg/kg) were found which improve within 1-2 days the conditioned activity of antenatally irradiated dogs.

17 PRESYNAPTIC DEPOLARIZATION OF TONGUE NERVE AFFERENTS. T.Akagi and N.Ishiko. Dept. of Physiology, Kumamoto Univ. Med. Sch., Kumamoto, JAPAN.

The anterior two-thirds of the cat's tongue comprises three receptive areas, each being innervated by one of three distal branches of the lingual-chorda tympani nerve bundle. The majority of somatic and gustatory fibers in the branches pass into the trigeminal component of the lingual nerve and chorda tympani, respectively. Primary afferent depolarization of these two kinds of sensory fibers was studied utilizing Wall's technique. An increase in excitability of the central terminals of each branch was observed in trigeminal nuclei. The magnitude and time course of the excitability change was found to relate to those of an inhibitory interaction among the evoked potentials produced by electrical stimulation of the three branches. The effect of stimulation to the branch nerves on the excitability of chorda tympani nerve terminals in nucleus tractus solitarius was not detected. The results indicate bulbar interaction between somatic afferents originated from different areas of the tongue. No interaction between gustatory afferents nor between somatic and gustatory afferents was found.

SPECTRUM OF THE INFRASLOW RHYTHMIC POTENTIAL OSCILLATIONS IN HUMAN AND ANIMAL BRAIN. N.A.Aladjalova, A.V.Koltsova, O.K.Koshtoyants. Inst.of Higher Nervous Activity and Neurophysiology, Academy of Sciences, Moscow, USSR.

The spectrum of the infraslow oscillations occupies the frequency range

intermediate between the (neurophysiological correlates of the) circadian rythm and the EEG-waves. Being classified according to criteria of their functional significance and the period the oscillations were grouped into five types with the periods: I) I,5-12 sec ("the second "waves), 2)15-6osec ("the deca-second"waves), 3)2-9 min("the minute"waves), 4)10-40 min ("the deca-minute" waves), 5) I-2 hours ("hour"waves). Continuus multichannel records were made from cortical, limbic and hypothalamic (HT) regions (rabbits) with chronically implanted electrodes and from the surface of the human head with non-polarizable electrodes (data on 70 subjects). Various types of rhythms may coexist in the same region. Also different types may occur in different regions simultaneously, the correlations however arising under some functional conditions. Several stages of the sleep were established as characterized by the waves transformation. Our understanding of the resultant HT activity provides an essential preliminary to studies concerned with any specific HT function. The problem of interpreting the peculiarities of the different components of spectrum must be considered in relation to brain autoregulatory mechanisms.

TRANSITIONAL CARDIAC CELLS IN THE ATRIO-VENTRICULAR REGION OF VARIOUS SPECIES. J. Alanís, D. Benítez, A. Martínez-Palomo, E. López. Dept. Physiology. Inst. Natl. Cardiología. México.

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The electrophysiological exploration of Purkinje-myocardial junctional region of the dog heart has revealed action potentials different in configuration from those generated by Purkinje or by ventricular cells. Under the electronmicroscope, distinctive morphological features were also observed. In the present study, transitional cardiac cells, identified both by their peculiar transmembrane potentials and ultrastructural features, have also been found in the atrio-ventricular region of several species, such as amphibia, reptilia and mammalia. The results suggest that a variation in the type and distribution of cell membrane contacts in the atrio-ventricular and in the Purkinje-ventricular regions, may be one of the structural factors responsible of the slow conduction velocities. The low rate of rise and the small amplitude of the action potentials generated by the transitional cells might be another factor contributing to the appearance of delays and blockages in conduction in the junctional cardiac regions.

THE NA⁺ ACTIVE TRANSPORT SYSTEM: PROPERTIES OF THE K⁺ ACTIVATION. R. W. Albers and G. J. Koval. Laboratory of Neurochemistry, NINDS, NIH, Bethesda, Md. 20014, USA.

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At the molecular level the active Na transport system seems to be a unit of the plasma membrane consisting of a Na dependent ATP-proteinphosphokinase and a K dependent phosphorylprotein phosphatase. The phosphatase will hydrolyse p-nitrophenyl phosphate. Dimethylsulfoxide (30% v/v) increases the phosphatase V about 10 x, reduces [K] 0.5V 7x and shifts the pH optimum from 7 to 9. K activation is sigmoid with Hill constant >2. Na (30 meq) converts K activation to hyperbolic form. Lower Na concentrations produce curves indicative of a mixed population of phosphatase molecules, some requiring single site and some, multiple site activation by K . Li will not replace Na . We conclude that phosphatase activation sites include one or more "non-specific" sites which accept either Na or K and one which will accept K but not Na .

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EFFECTS OF DISTENSION OF THE PULMONARY VEIN-LEFT ATRIAL JUNCTIONS IN DECER-EBRATE DOGS. S. Albrook & J.R. Ledsome. Dept. of Physiology, University of British Columbia, Vancouver, B.C., Canada.

Distension of the pulmonary vein-atrial junctions in anaesthetized dogs has been shown to cause stimulation of left atrial receptors and an increase in heart rate with little or no change in limb vascular resistance. This pattern of reflex activity differs from that of arterial baroreceptor reflexes the central connections of which are known to lie in the medulla. Dogs, anaesthetized with chloralose were decerebrated in the mid-collicular region using high frequency coagulation. Decerebration usually decreased heart rate and arterial pressure. Distension of the pulmonary vein-atrial junctions by means of small balloons caused a reflex increase in heart rate and there was no reduction in the magnitude of the reflex response after decerebration. The increase in heart rate was prevented by cervical vagotomy and markedly reduced by blocking doses of propranalol (0.5 mg/kg) given either before or after decerebration. Thus the reflex response was unaffected by decerebration and connections with the central nervous system rostral to the mid-collicular plane are not required for elicitation of the response.

EFFERENT INFLUENCES ON OLFACTORY PATHWAY OF CAT. C. Alcocer, H. 22 Aréchiga, H. U. Aguilar and R. Guevara. Dept. of Physiology, Sch. of Med. Natl. Univ. of México.

Evoked potentials were recorded at olfactory bulb (OB) lateral olfactory tract (LOT), olfactory tubercle (OT), prepyriform cortex (PPC) and anterior comissure (AC), stimulating at bulbo-mesencephalic reticular formation (RF) posterior hypoth alamus (PH) and medial forebrain bundle (MFB) of curarized cats. Evoked poten tials at OB are supressed after cutting LOT and electrolytically lessioning or tempo rarly blocking CT, but persist after AC or PPC lessions. Excision of both olfactory bulbs abolishes potentials at AC, without supressing those at other levels. Evoked potentials from RF are bilaterally recorded at all points of olfactory pathway, their latencies being equal for homologous structures at either side, and persist after longitudinally sectioning anterior and posterior commissures and corpus callosum. Conduction speed of efferent fibers at LOT is 5-10 m/sec. These data point to the existence of two parallel influences from non-olfactory areas upon the olfactory pathway, one to PPC and other to OT and OB. For the latter, OT acts as a final common pathway for the influences, both from olfactory and non-olfactory regions.

LUNG SURFACES: ALVEOLUS AND TRACHEA. I.G.S. Alexander, B.C. Ritchie, and J.E. Maloney, Depts. of Anatomy and Medicine, Monash Univ. and Dept. of Physiology, Univ. of Melbourne, Melbourne, Vic., Australia.

The alveolar and tracheal surfaces of the rat were studied with the scanning electron microscope. The alveolar surface appeared as an irregular network of ridges, which were shown by cross sectioning to be due to subepithelial capillaries. Epithelial cells covering alveolar vessels appeared clearly demarcated. The surface layer of the epithelium lining the trachea was comprised of ciliated brush and goblet cells as well as a cell, (collicular), which had a microvillous apex. Examined by transmission electron microscopy the collicular cell was found to contain a prominent endoplasmic reticulum and dense granules approximately lum in diameter. The relatively large number of collicular compared to goblet cells raised the possibility that the former may secrete a considerable proportion of the mucus in the trachea of the rat. A notable feature of the respiratory epithelium was the presence of brush cells each bearing approximately 100 long $(2\mu m)$ microvilli. These findings emphasize that symmetrical models of the pulmonary microcirculation may not be valid and that the functional interpretation of ciliated respiratory surfaces may require review.

VISUAL EVOKED RESPONSES OF THE CEREBRAL CORTEX ON DIFFERENT STAGES OF IN-24

DIVIDUAL DEVELOPMENT. V.V.Alferova, D.A.Farber.

Inst.of the Age Physiology. Acad.of Pedagogical Sciences, Moscow. USSR.

The analysis of the form and topography of the evoked visual potential
(EP) of the cerebral cortex of children from birth to 15 years of age showed that the primary complex of EP, reflecting the reception of qualitatively specific signal in projection zone of the cortex is formed in the postnatal period. Secondary components connected with the process of transformation of sensory information are formed later. In the period of birth the evoked visual response is recorded locally in the primary cortex and is represented by the positively-negative decline, indetified as components 2 and 3, (Ciganek) . Sometimes these components are preceded by early low amplitude components 0 and 1. Later components 4 and 5 can be clearly observed only from 5-6 years of age. Further evolution of visual EP in the projection cortex is manifested in reduction of time parameters of separate response phases with age together with the dynamics of EP in the visual cortex significant changes in its distribution can be observed From 5-6 years of age EP including its early components is registered in the non-projection cortical zone. Appearance of sensory-specific reactions outside the projection cortex reflects the involvement of the whole cortex in the analysis and coding of information, making possible the intersensory interaction RECENT STUDIES ON THE MYOID OF RODS AND COMES. M. A. Ali, Département de biologie, Université de Montréal, Case Postale 6128, Montréal 101, Canada.

The rods and cones of lower vertebrates such as fishes and frogs as well as those of some higher vertebrates such as some birds and mammals undergo positional changes in response to light and darkness. In light, the cones are contracted and the rods are expanded while the opposite occurs in the dark. This phenomenon has been much studied in so far as its characters are concerned (G. von Studnitz; Physiologie des Sehens, 2nd Edn. Akademische Verlagsgesellschaft, Leipzig, 1952; M. A. Ali, Actualités marines, vol. 8, 1964) but very little is known about the contractile mechanism. The myoid is the part of the cell which undergoes the most noticeable changes in length and sometimes, in diameter. In a histochemical and electronmicroscopic study of this part, we have failed to detect the presence of any contractile elements although the contractility of the rods and cones could be inhibited by Ouabain and PCMB. It appears that either the myoid has a primitive contractile mechanism such as what an amoeba may have, for example or, the site of contraction lies elsewhere in the visual cell. A new technique has been developed for the separation of living, visual cells from the fish and frog retinas and, using this technique we propose to study the myoid of the isolated cells by the glycerinated model technique and by a histochemical localisation of myosin like ATPases.

LIPID CIRCULATION AMONG TISSUES, BLOOD, LYMPH AND DIGESTIVE TRACT. A.A. Aliev. All-Union Research Institute of Physiology and Biochemistry of Farm Animals, Borowsk, USSR.

On the animals with cannulas in biliary and pancreatic ducts, with fistulas of stomach and intestine and also with catheters of portal and hepatic veins, carotid artery, lymphatic ducts it was found that there is continuous circulation of lipids among tissues, blood, lymph and digestive tract In ruminants two or three times more lipids than ingested with food are transfered from gissards to abomasum. The level of lipid secretion with bile and the synthesis of lipids in gissards are higher in animals with high level of fat in milk. Fatty acid composition of lipids in duodenal chyme, intestinal lymph, fat deposit and arterial blood is identical. The liver retains about 35 % of lipids entering with the blood. The retained lipids are partially metabolised and the rest is secreted with bile in the form of phospholipids and complex protein-lipid compounds. It is hepatic intestinal circulation of lipids. Arterio-venous differences in digestive tract blood shows that 8-14 % lipids are retained by the wall of digestive tract. Labelled lipids appear in the digestive tract following their injection into blood and fat deposits.

AFFERENT NERVE VOLLEYS ACTING ON DEITERS NEURONES VIA THE CEREBELLUM. G.I. Allen, N.H. Sabah and K. Toyama. Dept. of Physiol., State Univ. of New York at Buffalo, N.Y. 14214.

Deiters neurones receive excitation from collaterals of cerebellar afferents and inhib-

ition from Purkyne cells, and project directly to the spinal motoneurones. Thus, they provide the shortest route for cerebellar control of movement. The effects of ipsilateral fore- and hindlimb nerve stimulation upon Deiters neurones through the above-mentioned pathways were studied by means of intracellular recordings from barbiturate-anaesthetized cats. According to the location of the most effective nerve the neurones were classified as forelimb or hindlimb cells. In both types of Deiters neurones stimulation of the most effective nerve elicited an EPSP-IPSP sequence. All remaining nerves of the same limb (dominant limb) evoked a similar EPSP-IPSP sequence of smaller magnitude, or no response. On the other hand, stimulation of nerves in the other ipsilateral limb (nondominant limb) elicited only a long-lasting EPSP which was never followed by an IPSP of short latency. Latency and frequency depression of the response and excitability measurements of inferior olivary neurones during the response indicate that both types of response are relayed at the inferior olivary nucleus. It is suggested that there are two types of excitatory convergence onto Deiters neurones from the inferior olivary neurones; one is activated from the nerves of the dominant limb and always associated with the convergence of inhibition from Purkyne cells, and the other is activated from the nerves of the nondominant limb and entirely free from the inhibitory convergence of Purkyně cells. Antidromic identification performed on the two types of Deiters neurones revealed that about 85% of them project to the spinal motoneurones of the dominant limb while 15% to those of the nondominant limb.

PHYSIOLOGICAL DYNAMICS OF THE LOWER EXTREMITY. Robert D. Allison, Ronald H. Hayward, Robert N. Barnes. Scott and White Clinic and V. A. Medical Center. Temple, Texas.

Results of studies on healthy subjects, patients with diabetes mellitus and patients with peripheral arterial disease using the four electrode impedance plethysmograph have provided new insight into physiological mechanisms concerned with: 1) definition of lower limb "steady state" during exercise, 2) vasomotor response during postural stress, 3) superficial and deep vascular response to vasodilators and environmental temperature changes. Simultaneous ankle pressure and measured blood flow values to calf and foot segments before and immediately after exercise have defined the physiological segmental "robbing effect" that occurs during muscular exercise in the lower limbs. The results have been correlated with blood pressure, cardiac output and heart rate changes. In a similar manner, the resulting vasopressor responses to tilt table stress have been documented for evaluating orthostatic hypotension associated with diabetes mellitus. Preoperative and postoperative blood flow values and measured vascular responses to vasodilators have aided in the management of patients with peripheral arterial vascular disease.

29 K+ CONCENTRATION DECREASE IN THE T-TUBULES OF FROG SKELETAL MUSCLE DURING HYPERPOLARIZATION. W.Almers, Physiology Dept. Univ. Rochester, N.Y. U.S.A.

If there is appreciable K-permeability in the T-tubules, tubular [K*]should decrease when inward current is passed. During hyperpolarization, inward current is passed. During hyperpolarization, inward current is passed. During hyperpolarization, inward current indeed decays with time. To what extent is this effect due to tubular K*-depletion? Voltage-clamp experiments were carried out at 17-24°C on muscles immersed in a sulphate Ringer's fluid containing 10mM/1 K* and 10-7M/1 TTX. In this solution, only K* can carry appreciable membrane current. At the resting potential (RP), the ability to pass inward current recovered in two phases with half-times of about .02 and .5 sec, respectively; their relative contributions depend on amplitude and duration of the preceding hyperpolarization. After hyperpolarization, outward currents are seen at the RP which last a few seconds and indicate a small shift in equilibrium potential. Their time courses can be explained by assuming that tubular [K*]dropped by 50% or more during the hyperpolarization. It is concluded that the decay of inward current is due both to depletion of K* from the T-tubules and to a conductance change which occurs simultaneously. Fast and slow recovery, respectively, represent reversal of these two processes. On this basis, at least 60% of the K*-conductance has to reside in the T-tubules. Supported by NSF GB-15662.

CORRELATION BETWEEN THE RATE OF FALL OF THE ACTION POTENTIAL AND THE AMPLITUDE OF THE AFTERPOTENTIAL IN FROG SKELETAL MUSCLE. Wolfhard Almers and Clay M. Armstrong, Dept. of Physiology, Univ. of Rochester, N. Y., U.S.A.

Recent evidence indicates that the T-tubules can conduct action potentials. We have studied after-depolarizations (AD's) following action potentials (AP's) recorded from muscle fibers, attempting to identify a tubular contribution. Since the surface membrane depends on fiber diameter (d) and the area of the T-system on d², the latter's relative electrical contribution should increase with d. Using the input resistance (Rin) as a measure of d, we were unable to establish a correlation between Rin and either the AP's rate of fall or AD amplitude. We did find, however, a correlation between falling phase and AD amplitude. Fibers with slow falling phases had large AD's. After temporary exposuré to a solution containing 20mM K⁺, the falling phase was slowed and AD amplitude greatly enhanced. Insofar as the falling phase is a measure of the conductance of the delayed rectifier, these findings show that AD's are not the result of the delayed rectifier, but are caused by an as yet unknown ionic conductance with equilibrium potential positive to the resting potential by 40 or more millivolts. Supported by USPHS Grant NS-08951-03.

EXPERIMENTS SUGGESTING A COMMON ATP HYDROLIZING SITE FOR Na - AND (Na -K)-DEPENDENT REACTIONS. G. L. Alonso, O. R. Tumilasci and J. M. Nikonov. Dept. of Physiology, Sch. of Dentistry, Univ. of Buenos Aires, Buenos Aires, Argentina.

Rat brain microsomes with typical (Na -K)-dependent ATPase activity also show, at low ATP concentrations, a Na -dependent and K -independent ATPase activity.

Both enzimatic activities are inhibited by ouabain. While complete inhibition of Na -ATPase by ouabain takes place

immediately, a long incubation time was necessary to achieve complete inhibition of (Na -K)-ATPase.

This result, and differences in Mg/ATP ratio to obtain maximum activity in both reactions suggest that two different ATP hydrolizing mechanisms are operating, depending upon the presence or absence of K.

Inhibition of Na -ATPase by ouabain, in a short preincubation period, prevents further detection of (Na -K)-ATPase. This result suggests that a common enzyme system is involved in both reactions. a common enzyme system is involved in both reactions.

NEUROPHYSIOLOGICAL KNOWLEDGE PERTAINING TO LOCALIZATION OF A SOUND SOURCE IN SPACE. J.A. Altman. I.P. Pavlov Inst. of physiology, USSR Academy of Sciences, Leningrad, USSR.

The data are considered concerning the transformation of the afferent flow at different levels of the auditory system using interaural differences in stimulation with sound stimuli. At the first level of bilateral convergence (superior olive) the main reaction type of neurons is a monotonic reciprocal change of activity in the whole range of variation of interaural differences in stimulation; this allows to define both the side and the degree of the sound displacement from the midline. At the next level of the auditory system (inferior colliculus) this function is sharpened: the majority of neurons react with nonmonotonic changes of activity in a restricted range of interaural differences in stimulation; this nermits to defind more precisely the leastion of the sound of the sound. permits to defind more precisely the location of the sound. At higher levels (medial geniculate, auditory cortex) the information about the sound location is preserved in the sharpened form in the initial neuronal discharge; a subsequent processing consists in transformation of this information into short-term memory (changes of delayed discharges). Neurons-detectors of the sound motion direction are also described for different levels of the auditory system.

HISTAMINE-ANTIHISTAMINE ANTAGONISM IN ISOLATED ARTERIAL SMOOTH MUSCLE. Burton M. Altura. Departments of Anesthesiology and Physiology, Albert Einstein College of Medicine, Bronx, N. Y. U.S.A.

Evidence has accrued to suggest that at least four different classes of antihistamines (AH) have cardiovascular effects, in-vivo, over and above the property of histamine (H) antagonism (Am. J. Physiol. 218:1082, 1970). Furthermore, the ability of AH to antagonize the hypotensive and capillary actions of H in animals is rather limited when compared to their spasmolytic properties against H on bronchial and intestinal smooth muscles. These observations have led us to question the uniformity of the H receptor in smooth muscles (Am. J. Physiol. 209:545, 550, 1965). To our knowledge, there has been no acceptable demonstration of either a) a competitive-type of antagonism between AH and H on the effector smooth muscle cells in blood vessels, over wide dose ranges, as has been demonstrated for other types of smooth muscle or b) specificity of AH for the H receptor in vascular smooth muscles. Studies were therefore designed, using isolated rabbit aortic strips, to explore these phenomena. The use of complete cumulative dose-response curves and equi-molar concentrations (1.7x10⁻⁸M-8.6x10⁻⁴M) of five structurally different AH (e.g., diphenhydramine, chlorpheniramine, tripelennamine, pyrilamine and promethazine) reveals that: 1) true competitive H antagonism exists over very limited AH dose ranges; 2) non-competitive H antagonism is seen over rather wide AH dose ranges and 3) many AH can also antagonize certain other agonists (serotonin, acetylcholine, epinephrine) almost equally well.

These results must thus be considered in using AH as tools to define a physiologic or pharmacologic re sponse as histaminic in the cardiovascular system. (Supported in part by USPHS, NIH grants HE-12462 and HE-11391.)

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- THALAMOCORTICAL ORGANIZATIONS SUBSERVING CONTACT PLACING OF FORELIMB OF CAT. V.E. Amassian, H. Weiner and M. Rosenblum. Albert Einstein Col. of Med., New York, 10461, U.S.A. In chronic cats, placing (CP) after contact with dorsal, radial or ulnar aspects of paw starts with a withdrawal-lifting phase (Biceps and Flex. digit. EMG activity increased, prior Ext. digit. long. tone inhibited); subsequent loss of contact triggers a directed landing phase (Ext. digit. long. and Triceps activated. When the first phase of Biceps activity occurred early (eg 20-30 msec latency), it was often distinguishable from a later phase related to CP withdrawal. Ablation of motor cortex with medial surface with SI and variable amounts of SII results in loss of normal CP, but long-latency, stereotyped CP still occurs (rarely) to dorsal or medial contact; its incidence is markedly increased by tonic 100/sec red N stimulation, ipsilateral to the lesion. Evidence that sens rimotor cortex is part of a dynamic circuit subserving normal CP, rather than tonically facilitating a subcortical circuit includes: Large lesions of N ventralis posterior (VP) abolish CP to contact of specific contralateral sites. CP to contact of digits is spared unless ventral VP is destroyed. Recordings from individual VP and PT neurons during CP reveal responses early enough to initiate CP. However, the pathway skin-VP-sensorimotor cortex-lower motor centers is insufficient for CP. Thus, massive lesions of VL-VA that include ventral portions cause loss of CP (but release crossed CP) for eg 3 weeks, although large PT neurons are still powerfully activated by delicate contralateral stimulation. A minority of individual VL-VA neurons increase or decrease firing rates at various stages of CP; a few discharged early enough to be part of the dynamic circuit subserving normal CP. (Supported by USPHS grants NS-03491 & 01603.)
- ENERGETICS OF ISOMETRIC CONTRACTION IN THE FROG GASTROCNEMIUS MUSCLE. G. Ambrosoli, 35 P. Spiller and P. Cerretelli. Inst. of Physiology, University of Milano, Italy. When the muscle is stimulated tetanically in isometric conditions, energy (En) is released at the onset of the contraction (activation energy, corresponding to the activation heat, E_{n_A}) and during the maintainance of the tension (maintainance energy, $E_{n_{B+}}$): $E_{n_B} = E_{n_A} + E_{n_B}$. The energy has been measured from the high energy phosphates (\sim P) splitting and the lactic acid (L.A.) produced (given as \sim P equivalent) in the isolated frog gastroonemius. By stimulating the muscle in nitrogen with trains of tetanic impulses(20 cycles/sec at 10°C) of varying duration(1 to 6 sec) and at different i nitial length to obtain different tensions the activation and the maintainance energy could be determined. In the gastrocnemius the cost of maintainance of the tetanus En_{B+}) is not significantly affected by the tension developed. It amounts to about 0.45 μ Moles of \sim P per g of muscle and per second. The same results are obtained in experiments in which the muscles undergo a single tetanus of increasing duration. When the frequency of stimulation is increased from 20 to 30 cycles/sec, En increases from 0.45 to about 0.60 µMoles of ~P per g and per sec; the activation energy, En, which includes activation energy proper ,a', (3.5 mcal/g) and the energy corres ponding to the internal work (\overline{W}_{in}) , increases linearly with the tension developed.
- 36 TUBULAR REABSORPTION OF INORGANIC PHOSPHATE DURING SALINE DIURESIS. C. Amiel and H. Kuntziger. INSERM, Hôpital Tenon, Paris, France.

Increased urinary excretion of inorganic phosphate (Pi) during saline diuresis in the rat has been reported and assigned to the well documented decreased fractional reabsorption of glomerular filtrate (GF) in the proximal tubule. Tubular reabsorption of Pi during saline diuresis was studied by micropuncture technique. Saline diuresis was obtained by iv infusion of 0.15M NaCl at lµl/min/g body weight. Controls received the same solution at a 1/8 rate. The early distal and the late proximal superficial convolutions from the same nephron were both sampled. Results were obtained from 23 nephrons in 5 rats in the diuretic group and from 21 nephrons in 5 rats in the control one. The fraction of filtered Pi delivered at the end of the accessible proximal tubule did not differ significantly between the two groups despite a significantly higher fractional delivery of GF in the experimental one. Moreover, the difference between late proximal and early distal fractional Pi delivery per nephron was more than twice as high in the experimental ther in the control group (P<0.001) Finally fractional Pi excretion in ureteral urine was significantly lower in the experimental than in the control group. It is concluded that in superficial nephrons during saline diuresis : 1) the decrease in fractional proximal sodium reabsorption is not associated with a decrease in fractional Pi reabsorption and 2) there is an increase in net fractional Pi reabsorption between the late proximal tubule and the early part of the distal which could explain the decreased urinary Pi excretion.

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STIMULATION OF CONCOMITANT SECRETION IN VITRO OF LH AND FSH BY HIGHLY PURIFIED HYPOTHALAMIC LRF; EVIDENCE FOR A PROSTAGLANDIN RECEPTOR FOR THE RELEASE OF LH. M. Amoss, R. Blackwell, W. Vale, R. Burgus, and R. Guillemin. The Salk Institute for Biological Studies, La Jolla, California, U.S.A.

Highly purified (ovine) LRF has been purified following LH-releasing activity $\frac{\text{in vivo}}{\text{by}}$ a radioImmunoassay for rat plasma-LH. The LRF-activity is destroyed by incubation with a specific pyrrolidone-carboxyl-peptidase suggesting that LRF-activity is associated with a peptide with an N-terminal PyroGlu-. Addition $\frac{\text{in vito}}{\text{in a linear function}}$ by the pituitaries of 1.0;2.5;5.0;10.0 ng LRF/ml stimulate secretion of LH in a linear function with potency ratios respectively of 2.4;4.6;6.1;45.7. Concomitant measurements of FSH released in the same incubation fluids show potency ratios respectively of 0.9; 1.9;2.4;11.0. The activity of elevated $[\text{K}^+]$ in the $\frac{\text{in vito}}{\text{in vito}}$ system on stimulating release of LH is inhibited by preincubation with the prostaglandin antagonist 7-oxa-13-prostynoic acid (3.10⁻⁵ M). These results question though they do not disprove the existence of a specific FRF different from LRF which others claimed to have separated at much earlier stages of purification than the one achieved here; they also expand to LH our earlier results (Fed. Proc. $\frac{30}{2}$, 1971) proposing the involvement of a prostaglandin receptor in the mechanisms of secretion of other (TSH,ACTH) anterior pituitary hormones.

A COMPARATIVE STUDY OF GASTRIN CONTENT IN EQUINES AND RUMINANTS. B. O. Amure Department of Physiology, University of Ibadan, Ibadan, Nigeria.

Recent studies have shown that gastrin can be extracted in its crude form from the gastric antra of animals. This is then subjected to partial or complete purification and tested both quantitatively and qualitatively. It has been shown recently that herbivores have relatively large store of gastrin in their gastric antra when compared with carnivores or omnivores. In view of the fact that this finding may be related to dietary habits, further investigations into the gastrin content of equines (horses and donkeys) and ruminants (sheep and goats) were conducted. The results showed that the equines have a large store of gastrin when compared to ruminant animals. Both equines and ruminants have larger yields of crude gastrin powder than carnivores (dogs and cats) or omnivores (pigs and man). These findings further confirm the influence of dietary habits on the gastrin content of gastric antra in animals.

MECHANICAL FACTORS AFFECTING BARORECEPTOR FUNCTION. I.S. ANAND and D.H. BERGEL. University Laboratory of Physiology, Oxford, U.K.

The effect of constricting the carotid sinus wall of the dog by perfusion with blood containing noradrenaline at a concentration of 1 mgm/L is generally to make the single fibre baroreceptor unit less sensitive at low pressures and more sensitive at higher pressures. The magnitude and the time course of accommodation following a step change of pressure are also altered. Parallel measurements of pressure volume relationship and of stress relaxation in the common carotid artery before and after smooth muscle activation suggest that this is related to the mechanical properties of muscle wall.

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THE EFFECT OF SHORT-LASTING REPETITIVE VIBRATION OF THE TENDON OF TRICEPS MUSCLE AND CONCOMITANT FUSIMOTOR STIMULATION ON THE REFLEX RESPONSE OF SPINAL ALPHA MOTONEURONES IN DECEREBRATED CATS. Radmila Anastasijević M. Cvetković and J. Vučo. Inst. for Med. Res., Belgrade, Yugoslavia.

Short lasting repetitive vibration of the muscle tendon with peak to peak amplitude from 29 to 289µ produced an increase in the discharge of motoneurone reflex spikes and the size of extensor monosynaptic reflex in comparison to their reflex response established during continuous vibration, lasting the same time as the interrupted one. Fusimotor stimulation, synchronous with periods of vibration in the repetitive series, produced an additional increase in reflex firing without changing the already established reflex response pattern of motoneurone units. Series of repetitive vibration and concomitant fusimotor stimulation with pauses between stimuli lasting 1800 and 1000 msec had, in comparison to the other series, considerable excitatory action on reflex response of both motoneurone units.

41 ANGIOTENSIN - SODIUM INTERACTION IN CENTRAL CONTROL OF FLUID BALANCE. B. Andersson, L. Eriksson, O. Fernández and R. Oltner. Dept. of Physiol., Royal Veterinary College, 104 05 Stockholm, Sweden.

Infusions of hypertonic NaCl solution into the 3rd brain ventricle of the goat elicit drinking, natriuresis, and release of antidiuretic hormone (ADH). The latency time for drinking is brief when the infusions are made into the anterior part of the 3rd ventricle (1 to 3 min). These effects of NaCl were markedly potentiated when angiotensin (0.5 - 1 ng/kg/min) was added to the infusion of hypertonic saline. Thirst, inhibition of water diuresis and increased renal Na⁺ excretion was also obtained to some extent by the infusion into the 3rd ventricle of angiotensin dissolved in isotonic or slightly hypotonic saline. However, angiotensin infused into the 3rd ventricle in iso- or hypertonic solutions of sucrose or glucose had no or very little dipsogenic, antidiuretic and natriuretic effect. Infusions of hypertonic NaCl and angiotensin into the 4th brain ventricle did not affect the fluid balance of the goats significantly. A possible explanation for the results may be that Na⁺ sensitive receptors, which are influenced by the Na⁺ concentration of the cerebrospinal fluid, are located near the wall of the 3rd ventricle, and that these receptors participate in the regulations of thirst, ADH release, and renal sodium excretion. The observed angiotensin – Na⁺ interaction indicates that angiotensin either make such receptors more sensitive to the environmental Na⁺ concentration, or in some manner increases the exposure of the receptors to Na⁺. This work was supported by the Swedish Medical Research Council (projects no B71–14X–503–07B and B70–99F–3054–01).

42 FIRING PATTERNS INDUCED IN VPL CELLS BY PERIPHERAL AND CORTICAL STIMULATION. S. Andersson and M. Takata. Dept. of Physiology, Univ. of Göteborg, Sweden.

Extracellular and intracellular recordings have been made in nucleus ventralis posterolateralis (VPL) during light barbiturate anaesthesia or in unanaesthetized, partly decorticated cats. The cellular potentials were studied with regard to activity occurring spontaneously or induced by electrical stimulation of peripheral fields and the somatosensory cortex. The induced activity showed a large variability in various cells, particularly in cells which appeared to be interneurones. In such cells cortical stimulation gave excitation or inhibition or a combination of these effects, whereas peripheral stimulation mainly elicited excitation. The main post-stimulus variation in the relay cells occurred in the IPSP following the cellular discharge. The spontaneous discharge of the relay cells was often completely blocked by repetitive cortical stimulation whereas peripheral stimulation gave EPSP-IPSP sequences. It was observed that spontaneous spindles could be enhanced by cortical stimulation but blocked or shortened by peripheral stimulation.

REGULATORY CHANGES IN RESPIRATION CAUSED BY PROLONGED DUST EXPOSURE.

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Significant changes were observed in respiration after prolonged dust exposure. Changes in lung volumes and in the mechanical properties of the lungs were associated with abnormal regulation of breathing. The effect of CO₂ and O₂ breathing on the ventilation of coalminers exposed for years to dust was investigated. The inhalation of a gas mixture containing 5 % CO₂ in air caused a smaller increase in ventilation than in healthy subjects. The reduced response to CO₂ was connected with increased work of breathing. The effect of CO₂ depends on the O₂ tension of the alveolar air, being smallest in pure O₂. The inhalation of 100 % O₂ does not reduce the ventilation of men exposed to dust for years. In moderate exercise (75 W) a very small reduction of O₂ content in the inspired air (19 %) significantly increased ventilation, and consequently the quantity of dust inhaled.

EFFECTS OF STEROID HORMONES ON THE SYNTHESIS AND RELEASE OF CORTICOSTEROIDS BY ORGAN-CULTURED HAMPSTER ADRENAL GLANDS.* R.V. Andrews, Dept. of Biol., Creighton Univ., Omaha, NB 68131, U.S.A.

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Culture techniques have been employed in our laboratory to investigate circadian rhythms in adrenal function which persist in vitro. The observations that (1) phase-shifting adrenal secretory rhythms could be effected by pulse-doses of ACTH given out of phase with the control cycle, and (2) that progesterone levels (intracellular and secreted) are increased by ACTH pointed to end-product inhibition as a possible factor in autorhythmic function of the cultured adrenal gland. While exogenous doses of cortisol and corticosterone did not modify their own in vitro secretory rhythms, doses of progesterone did attenuate the phase and amplitude of rhythmic secretion of the corticosteroids. When progesterone was delivered in-phase with the secretory peak, marked inhibition of cortisol and corticosterone synthesis and release was recorded, while stimulation was observed when progesterone was delivered during the low point in the cycle. The level of adrenal progesterone appears to depress synthesis and secretion of corticosteroids during the secretory peak; the appearance of the peak can be blocked and delay phase-shifted by treatment with progesterone delivered during the rising phase of the secretory cycle. *Supported by NSF Grant GB-8307.

CENTRAL PROJECTIONS OF SUPERIOR LARYNGEAL NERVE. I.S. Aneia and S.K. Manchanda. Dept. of Physiology, All India Inst. Med. Sci., New Delhi, INDIA

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Stimulation of the internal branch of the superior laryngeal nerve (SLN) in the cat evoked two types of responses in the medulla oblongata. 1: Short latency and short duration primary responses were localized in the tractus solitarius and its nuclei, dorsal motor nucleus of vagus, medial longitudinal fasciculus and in the reticular formation ventral to tractus solitarius. Recording at the SLN exhibited antidromic responses on stimulation of all these regions except the medial longitudenal fasciculus. These responses were obtained only ipsilaterally. 2: Long latency, long duration secondary responses were obtained from reticular formation both ipsilaterally and contralaterally, and from the vagal commissure. The area of secondary responses extended medially and ventrally upto one mm. dorsal to the inferior olive and rostro-caudally from obex to 5 mm above it. Stimulation of lateral hypothalamic area markedly potentiated the SLN evoked secondary responses without affecting the primary responses. Stimulation of the SLN is known to evoke reflex swallowing which is complete in all its components. This study therefore delimits the medullary areas involved in the neural organization of the swallowing reflex and establishes the potentiating effect of lateral hypothalamic feeding area on this reflex.

ADRENERGIC INNERVATION AND ADRENERGIC RECEPTORS OF THE BLOOD VESSELS OF THE HYPOTHALAMUS. E. T. Angelakos, M. P. King and L. Carballo. Dept. of Physiology & Biophysics, Hahnemann Med. Col., Philadelphia, Pa. U.S.A.

Extensive adrenergic innervation was found in the vessels of the hypothalamus in a variety of species studied (rat, rabbit, hamster, cat, squirrel monkey) using fluorescence histochemical techniques. Similar innervation was found in the pia vessels but was lacking in vessels of the cortex. The vascular innervation degenerated after chronic bilateral superior cervical ganglionectomy (cat) and seemed to account for 25 - 30% of norepinephrine (NE) present in the hypothalamus. Evaluation of rapid (3 min) and late (45 min) uptake and binding of H³ NE in the presence and absence of alpha and beta adrenergic blocking drugs indicated the presence of both types of adrenergic receptors in the hypothalamic circulation. By contrast alpha receptors seem to predominate in the pia vessels while beta receptors are predominant in the circulation through the cortex. It is concluded that the adrenergic control of hypothalamic vessels may be quite different than that found in the cortex or reflected in measurements of total cerebral blood flow.

47 EEG AND RT CHANGES UPON DIFFERENT LEPTOCURTIC FOREPERIOD DISTRIBUTIONS.
A. Angelov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia,
Bulgaria.

EEG and RT changes were investigated simultaneously when 6 equally spaced foreperiods were varied randomly, ranging from 0,50 to 1.50 sec under three different leptocurtic foreperiod distributions: I - the maximum foreperiod, 1.50 sec, was repeated 12 times more than the rest; II - the minimum foreperiod, 0.50 sec, was the most frequently occurring foreperiod; III - the 1.10 sec foreperiod was the most frequently occurring one. The length of the foreperiods were measured by two consecutive flashings of a flashlamp. The EEG from both the visual and motor regions was recorded. The relationship among the evoked EEG alphablocking, the foreperiod duration, the probability of stimulus occurrence and RT was studied. Under the conditions of the three leptocurtic foreperiod distributions (I,II,III) differences were established in the shape of the RT-foreperiod curves as well as in the values of both latency and duration of the alpha-blocking evoked by the warning signal.We suggest that the changes observed of the evoked alpha-blocking parameters are related to the information content of the stimulus.

ALTERATIONS IN BLOOD PRESSURE, HEART RATE AND RESPIRATION DURING SELF-STIMULATION IN THE CAT. L. Angyán, S. Rác and E. Grastyán. Inst. of Physiology, Univ. Med. Sch., Pécs, Hungary. Arterial blood pressure, heart rate, respiration and the hippocampal

Arterial blood pressure, heart rate, respiration and the hippocampal electrical activities were continuously recorded in 6 cats during self-stimulation with electrodes implanted in the hypothalamus and in the thalamus. The effects of different parameters of electrical stimuli were also studied before and after bilateral vagotomy. A consistent acceleration in heart rate and respiration was obtained during stimulation. The changes in blood pressure were, however, different depending on the animal and the stimulated point: in certain cases an increase, in the others a decrease or biphasic effects were recorded. The threshold of the blood pressure effects was regularly higher than that of the self-stimulation. A considerable diminution of the effect or no alterations were found during lever-pressings when the electrical stimulation was omitted. The relative importance of central and peripheral regulatory mechanisms in the production of the described manifestations is discussed.

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DECREASE OF PO 4-UPTAKE BY QUABAIN IN MAMMALIAN NON-MYELINATED NERVE FIBERS.
Béatrice Anner and R.W. Straub. Inst. of Pharmacology, Univ. of Geneva, Switzerland.

Desheathed rabbit vagus nerves were incubated in Tyrode containing $^{32}\text{PO}_4$; the uptake of PO $_4$ was measured as well as its incorporation into some nucleotides, after separation by thin layer chromatography. The uptake of PO $_4$ reached saturation after 15 min. Addition of iodoacetic acid (IAA) or 2-deoxyglucose (2DG) to glucose-free Tyrode was found to decrease the uptake of PO $_4$ by about 2O% and its incorporation into ATP, ADP and GTP. A similar decrease in the uptake of PO $_4$ was found when ouabain was added to Tyrode; in this case, however, the incorporation into the nucleotides remained unchanged. While these experiments suggest that the uptake of PO $_4$ is decreased by ouabain when the Na-K-pump works in the forward direction, other experiments showed that a decrease is also found when working of the Na-K-pump is reversed. In preparations that were previously incubated into K-rich, Na and glucose-free Tyrode to which either IAA or 2DG had been added - and subsequently transferred to Na and $^{32}\text{PO}_4$ rich, K and glucose-free Tyrode with the same inhibitors - the addition of ouabain also decreased the PO $_4$ uptake. These experiments suggest that transport of PO $_4$ accompanies the working of the Na-K-pump in the forward and backward direction.

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A HYPOTHESIS OF NEUROPHYSIOLOGICAL AND NEUROCHEMICAL MECHANISM OF CENTRAL ACTION OF PSYCHOTOMIMETIC DRUGS. I.P.Anokhina, T.T.Bondarenko, N.A.Khristoliubova. Central Research Institute of Forensic Psychiatry, Moscow, USSR.

In the present study an attempt has been made to clarify the mechanisms of central action of psychotomimetic drugs (LSD, marihuana etc.). The data were obtained by means of acute and chronic animal experiments. The following procedures were utilized in various CNS regions:1) registration of general EEG and single neuron discharges;2) microinjections;3)determination of biogenic amine levels;4)examinations of MAO activity and biogenic amine intracellular content. These investigations were carried out concurrently with observations of behavior responses. Simultaneous interactions between psychotomimetic drugs and certain substances influencing synaptic transmission were studied. Administration of the psychotomimetics produced the most marked changes in the activity of adrenergic and serotoninergic structures of the mesencephallic RF and in the limbic system. It is assumed that the drugs interfere principally with the biogenic amine metabolism in individual nerve cell groups of the mesencephalic RF. Local disturbances produced by the drugs cause a number of secondary changes in the CNS activity accompanied by behavioral alterations. Since functional changes arising in a limited number of neurons produce extensive pathological alterations in the CNS functions it may be concluded that the "pacemaker" mechanism (P.K. Anokhin) is underlying the effect of psychotomimetic drugs.

KINETICS OF THE TRANSPORT OF NON-ELECTROLYTES BY THE RAT INTESTINE IN VIVO. J.-A. Antonioli and J.W.L. Robinson, Pharmacologie Clinique, Clin.Méd.Univ., et Chirurgie Expérimentale, Clin.Chir.Univ., Lausanne, Suisse.

Transposition in vivo of kinetic models developed in vitro is fraught with problems. Perfusion studies were carried out in situ in anaesthetised rats, and isotopic, chemical and chromatographic analyses were performed on the perfusate and the intestinal tissue, in an attempt to evaluate kinetic parameters for phenylalanine, lysine or galactose absorption. Using a continuous recirculating perfusion technique, the velocity of uptake for all substrates was found to be directly proportional to the substrate concentration over a 1000-fold range, and the absolute transport velocities were much lower than those found in vitro. Furthermore, the interactions between several amino-acids were much less than expected on comparison with in vitro results. On the other hand, when perfusions without recirculation were performed, initial uptake velocities similar to those obtained in vitro were observed, but a steady-state was attained within a few minutes. The results indicate that the absorption systems in vivo are very rapidly saturated, after which the substrates are absorbed by non-saturable mechanisms with low transport velocities.

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52 BEHAVIOURAL AND EEG CHANGES FOLLOWING MELATONIN ADMINISTRATION TO HUMANS. F.Antón-Tay. Inst.de Investigaciones Biomédicas, UNAM México 20, D.F.México.

Melatonin (5 methoxy-N-acetyltryptamine) is a hormone synthetized in mammals only by the pineal gland. The administration of this methoxyindol to experimental animals is followed by striking EEG and metabolic changes. However, the effect of this hormone in humans is unknown. During the last year, we have been studying the effects of administered melatonin to healthy, parkinsonian and epileptic subjects. In all cases an increase of EEG alpha activity, sleep, imaginary, a feeling of well-being and elation was found. In epileptic patients, a decrease of the paroxystic graphoelements was also noticed. Chronic administration of melatonin to parkinsonians was followed by general improvement of the sindrome.

QUANTITATIVE HEAT CLEARANCE FOR LOCAL BLOOD FLOW MEASUREMENT. H. Apfel, E. Betz, W. Müller-Schauenburg. Inst. of Physiology, Tübingen.

We have derived the following equation separating heat conduction from heat convection by blood flow:

 $\ln \frac{\partial}{\partial t} \vartheta(t, \frac{\phi}{\lambda}) - \ln \frac{\partial}{\partial t} \vartheta(t, 0) = -\frac{\phi}{\lambda} (t - t_0)$

where $\frac{\partial t}{\partial t}$ denotes time differtiation. \Re means the temperature field of locally applied heat depending on the time t, the blood flow φ and the partition-coefficient (blood/tissue) λ of heat after switching on or switching off the heat power supply at the time $t=t_0$. If the left side of the equation is plotted versus $\frac{t_0-t}{\lambda}$ a straight line results, the slope of which is a measure of local blood flow (ml/g·min). A resistance bridge with heated microthermistors is demonstrated. The device allows to record the time course of \Re at two sites of the tissue and the temperature difference $(\Re - \Re)$ between the thermistors. An analog- or digital computer may be connected with the output of the power supply for automatic calculation of φ .

54 INTERFERENCE OF THYROID HORMONES IN THE BIOCHEMISTRY OF DEVELOPING RAT BRAIN. Alexandra Ardeleanu, Maria Stefan and N.Sterescu, "D.Danielopolu" Inst. of Physiology, Academy of Medical Sciences, Bucharest, Romania.

Starting from the assertion according to which the rat is a postnatal brain developer (Davison and Dobbing) being very sensitive to hormonal influences during the most intensive period of development of its central nervous system, the author carried out a dynamic study concerning the influence of I-triothyronine (T2 and D,I-thyroxine (T4) on 32-P -incorporation into cerebral phospholipids and on the activity of some brain enzymes (catalase, pyrophosphatase and ATP-ase) in new-born rats of either sex. Following a brief period of more reduced rate of 32-P-incorporation into brain phospholipids, the treated group presented a significant stimulation of this process in the subsequent steps of the experiment. After 7 days of treatment, T2 and T4 also determine a marked rise in catalase activity, this effect being reduced in the subsequent phases; by the end of 21 days the values approximated those of controls. A stimulating effect though shoter and less accentuated -was noted in brain pyrophosphatase and ATP-ase activity following T2 and T4 treatment. The authors discuss the significance of the results which point to the role of thyroid hormones in the process of myelinization of the developing rat brain.

ON THE NATURE OF CIRCADIAN RHYTHM OF ACTIVITY IN CRAYFISH NERVOUS SYSTEM. H. Aréchiga, B. Fuentes, B. Barrera and L. F. Abreu. Dept. of Physiology, Sch. of Med., Natl. Univ. of México.

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The electrical activity of single neurons in the crayfish, as lead by chronically implanted microelectrodes, shows circadian variations with a diurnal phase of low reactivity and a nocturnal phase of high reactivity. Such variations have been recorded at various levels of neural integration. 1) Primary receptors, as retinal photorreceptors, whose response to light is two to four times greater during nocturnal phase. 2) Interneurons whose spontaneous activity and response to specific sensory input are higher during night, their rate of habituation under repetitive stimulation being lower. These variations are similar in visual than in non-visual interneurons. 3) Motor neurons spontaneous activity. Extracts from sinus glands, visual ganglia or supraoesophagic ganglia which promote migration of retinal shielding pigment towards light-adapted position, depress the activity of neurons at all the aforementioned levels. These results indicate the existence of a uniformly acting humoral modulation of neuronal activity, exerted through the sinus gland and whose predominant effect is to induce the diurnal phase of circadian rhythm.

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RESPONSE OF ANAL CANAL TO THE RECTAL DISTENSION. P. Arhan, Cl. Favordin, J.-L. Parrot, J. Thouvenot. Chaire de Physiologie, Faculté Necker, Paris, France.

In the course of research on anal continence, the motility of anal canal has been studied in normal children aged from three months to 13 years. Variations of tonus of anal canal were estimated following the volume of distending balloon.

EFFECT OF ADMINISTRATION OF LH-RH ON SERUM LH AND PROLACTIN LEVELS IN HYPOPHYSEC-TOMIZED FEMALE RATS BEARING A PITUITARY GRAFT. ULTRASTRUCTURAL STUDIES OF THE PITUITARY GRAFT. A. Arimura, E.G. Rennels, M. Shiino, and A.V. Schally. Dept. Med., Tulane Univ. Sch. Med., and VA Hosp., New Orleans, La., and Dept. Anatomy, Univ. of Texas, Med. Sch. San Antonio, Texas, U.S.A.

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Effect of acute and chronic administration of a highly purified luteinizing hormone-releasing hormone (LH-RH) of porcine origin on the serum LH levels was studied in hypophysectomized female rats bearing a pituitary graft, which was transplanted 1 month before the experiment. Serum LH and prolactin were determined by radioimmunoassay. Mean resting levels of serum LH in these animals ranged from non-detectable to .95 ng/ml, expressed as NIH-LH-S-7. Serum LH increased 17 fold after 0.3 µg LH-RH was infused iv over 30 min. Saline infusion did not change serum levels significantly. Intra-aortal infusion of 0.1 µg LH-RH in these rats also increased serum LH from non-detectable to 3.1 ng/ml. Serum prolactin levels did not change significantly after infusion of LH-RH. Some hypophysectomized rats with a pituitary graft were continuously infused through the implanted cannula with 5 µg LH-RH/day, or saline for 1 week. The graft was then removed for ultrastructural studies. Electronmicrographs showed presence of many healthy Kurosumi's LH cells in the grafts from LH-RH infused rats. GH cells were also present, but it was more difficult to differentiate those cells from LH cells than in intact pituitaries.

CLASSIFICATION OF NORMAL AND PRE-PATHOLOGICAL STATES OF THE CARDIO-VASCULAR SYSTEM. N. I. ARINCHIN. Gerontology Sector, Byelorussian Academy of Sciences, Minsk, USSR.

In contrast to the pathological, the normal and pre-pathological state of blood circulation has no classification. It has been established by various methods in more than 100 representatives of 11 orders of 2 classes of birds and mammals that average arterial pressure (AP) is maintained by various mechanisms; in small animals, by high total peripheral resistance (TPR) with low minute blood circulation volume (MBCV) - the vascular type; in large animals by high MBCV and low TPR - the cardiac type; in man by MBCV and TPR equally - the average type of self-regulation of blood circulation. Further classification of normal blood circulation for identical AP in healthy humans can be made by comparing proper values of PMBCV and PTPR with actual values. Thus average (values of MBCV and TPR coincide or do not exceed sigma, i.e. 10% of PMBCV and PTPR), cardiac (MBCV higher than PMBCV) and vascular (TPR higher than PTPR) types of self-regulation of blood circulation are revealed. The average type is the most reliable, and the others with still greater divergence of actual from proper values of MBCV and TPR, are very probable sources of pre-pathological and pathological states.

59 IN SITU PAPILLARY MUSCLE FUNCTION. J.A. Armour and W.C. Randall. Dept. of Physiology, Loyola University Medical Center, Maywood, Illinois, U.S.A. Coarctation of the aorta or pulmonary artery is accompanied by increased intraventri-

Coarctation of the aorta or pulmonary artery is accompanied by increased intraventricular pressure, distension of ventricular musculature, and elevated epicardial contractile force. Concomitant measurements of force from Walton-Brodie strain gauge arches sutured to papillary muscles in both ventricles revealed only minimal change or decrease in force. In contrast, direct inotropic stimulation elicited a marked increase. Graded addition of weights to the chordeae tendineae of in situ papillary muscles in the spontaneously beating heart (with or without complete cardiac bypass) was performed while recording length and force of the papillary muscle together with alterations in force on distant epicardial segments. Arrhythmias similar to those accompanying severe venticular distension were readily induced by elongation of a papillary muscle. These were modified and often abolished by bilateral cervical vagotomy. Little or no augmentation in force of papillary muscle contraction accompanied increased load; rather force decreased. Extrinsic cardiac denervation resulted in modification of these responses to papillary muscle stretch. Intrinsic denervation elicited a force-length curve showing prominent ascending and descending limbs. Force recordings from distant epicardial segments were frequently augmented with increasing papillary muscle length, this relationship showing definite attentuation after intrinsic denervation. Thus, local "reflex" effects between different regions of the heart via "neural" arcs may play important roles in cardiac control. (Supported by Grant HE 08682 from NIH, USPHS).

60 EFFECT OF ADENOSINE TRIPHOSPHATE (ATP) ON TRANSMURAL P.D. AND SHORT CIRCUIT CURRENT IN ISOLATED BULLFROG SMALL INTESTINE. W. McD. Armstrong and G. A. Gerencser. Indiana Univ. Sch. Med., Indianapolis, Indiana, U.S.A. 46202.

ATP is known to induce transient increases in transmural P.D. and short circuit current (S.C.C.) in isolated mammalian small intestine. When sheets of bullfrog small intestine are mounted in an Ussing chamber between identical isotonic sodium sulfate Ringer solutions (in which net mucosal to serosal sodium transport and S.C.C. are equal), ATP (5 mM) added to the mucosal medium causes sustained reversible increases in S.C.C. and transmural P.D. Both parameters increase in parallel (i.e. steady state tissue resistance is unchanged) and both are unaffected by serosal ATP. The response to mucosal ATP is obtained when metabolism is inhibited by nitrogen, 2,4-dinitrophenol, or sodium fluoride. It is inhibited by serosal ouabain. Mucosal adenosine diphosphate (ADP; 5 mM) does not affect transmural P.D. or S.C.C. in the absence of ATP, but completely inhibits their response to mucosal ATP. The ATP response is unaffected by actively transported sugars or amino acids added to the mucosal medium and is not inhibited by phlorizin. These results suggest that the response of transmural P.D. and S.C.C. to mucosal ATP involves direct interaction of this compound with a component of the sodium transport system in bullfrog intestine (possibly a Na-K specific membrane ATP-ase) which is accessible to exogenous ATP in the mucosal but not in the serosal medium. (Supported by USPHS Grants AM 12715 and HE 06308)

HEMORHEOLOGY IN THE PULSATILE MICROCIRCULATION. J. Aroesty and J. F. Gross. Department of Environmental Sciences, The Rand Corporation, Santa Monica, California, USA.

Recent experiments have indicated substantial regions of pulsatile flow throughout the microcirculation extending from the arterioles to the venules. In the capillaries, where two-phase flow is present, several analyses have treated the rheological properties of individual erythrocytes interacting with the plasma in unsteady motion. As the scale of motion increases, corresponding to flow in the arterioles and venules, a continuum model, which reflects the results of recent <u>in vito</u> experiments, is proposed. Whole blood, when flowing in small diameter vessels, is assumed to separate into a core which behaves like a Casson fluid and an annular region near the wall whose viscosity and thickness are de-

rived from in vitro steady experiments. Observations indicate that the wall layer is constantly being penetrated by individual cells from the core which contribute to momentum transfer and, therefore, the viscosity of the wall fluid is different from that of plasma. It has been shown that quasi-steady approximation to pulsatile flow is sufficiently accurate to describe unsteady flow in small vessels when the Womersley number is small. This approximation is incorporated into the model to investigate the effects of wall layer, core properties, hematocrit, and vessel elasticity. The single vessel model is then integrated into a network simulating the unsteady flow behavior in a single organ.

IMPAIRMENT OF ADRENERGIC FUNCTIONS BY TETANUS TOXIN. Satish Arora, M.L. Dave & R.K.Snyal. Dept. of Pharmacology, Maulana Azad Med. Col., New Delhi, India.

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The tetanus toxin produced a systemic pressor action, a positive chronotropic and inotropic effect on the heart and a reduction of peripheral blood flow in several species of animals. It also produced a contraction of the dog splenic capsule and guinea-pig vas deferens. There was a transient hyperglycaemia when the tetanus toxin was given to fasting dogs. The cardiac effects were absent after B-adrenergic blockade. The peripheral vasoconstrictor action was either absent or reduced after phenoxybenzamine and in reserpinised animals. In the rat the pressor action was annulled after phenoxybenzamine and potentiated after ganglion blockade. When catecholamines stores were depleted by giving ephedrine repeatedly till tachyphylaxis to its pressor action was produced, tetanus toxin failed to cause a rise in blood-pressure. Similarly the pressor action was absent in rats treated chronically with imipramine to block the uptake of catecholamines by the stores. The action was unaltered after adrenalectomy. The above experiments indicate that the tetanus toxin produces a sympathomimetic action very likely by releasing catecholamines from peripheral storage sites.

EFFECTS OF CYCLOPROPANE ON CARBOHYDRATE TOLERANCE. J.C.Arraga. Dept.of Physiology. Med. Sch. Univ. of Zulia. Maracaibo. Venezuela.

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It has been reported a diminution of carbohydrate tolerance in the initial days following surgery or trauma, as a part of metabolic response to injury. In twelve patients undergoing elective surgery, I have practiced the intravenous glucose tolerance test 24 hours before and 24 hours after surgery, wich was done under general anesthesia with cyclopropane and oxigen; a statisticaly significant tolerance diminution in latter test, as compared with the former, was observed (P < 0,01). To determine the part that could be played by anesthesia, I have studied two groups of rats:(1) each animal was placed, during 1 hour, inside a closed circuit (animal chamber with CO2 absorber, connected to a spirometer containing air; (2) animals were similarly treated, but breathing a mixture of cyclopropane (33%) and air (77%); after initial 15 minutes, cyclopropane concentration was increased in 15%; animals slept but they were easily awaken. At the end of period all animals were killed, liver removed, refrigerated, and glycogen content determined. Average content in second group was 31,7% lower than in control group (P<0,01). It appears that not only accidental or surgical injury may be causative agent of metabolic response; in the absence of wurgery, the anesthetic, by inself, can produce effects on carbohydrate metabolism; it has been known that cyclopropane increases blood catecolamine levels, but may also exist different mechanisms not suggested by these experiments

The author wish to acknowledge the technical assistance of A.Camizales.

THE DIFFERENT SENSITIVITY OF THE ATRIOVENTRICULAR NODE CELLS OF RABBIT TO ACETYLCHOLI NE AND MORADREMALINE APPLIED BY MICHOIONTOPHORESIS. I. Arrigo, G. L. Avanzino, R. Ermirio 64 and S. Ciangherotti. Istituto di Misiologia Umana, I and II Cattedra, Università degli Studi, Genova, ITALIA.

The effects of neurotransmitter substances at the level of the atrioventricular node have been long studied in the attempt, also, to clarify the mechanism of the spread of the excitation trough such area. This type of research is complicated by the peculiar anatomo-functional organization of the atrioventricular node area which cells seem to be disposed in several successive rows affecting each other. The micro iontophoretic method allows one to apply Acetylcholine or Noradrenaline on very limi ted areas and, in the case of the atrioventricular node, to study the effects of such substances on the fibers under normal activation by the neighbouring cells. The microiontophoretic application of Acctylcholine provoked in most of the transitional atrionodal or definitely nodal cells the appearance or the increase of two or more components in the upstroke of the action potential, the delay in the appearance of his later components could also be appreciated. Noradrenaline provoked some times op posite effects. The various types of responses were divided in groups according to the position of the fibers and to the relative time of activation.

INVESTIGATION ON THE ELECTRO-CONTRACTILE COUPLING OF FROG VENTRICULAR STRIP CONCERNING CALCIUM, SODIUM, NOREPINEPHRINE, INDERAL, STRETCH AND THEIR RELATIONSHIP. Gh.Arsenescu, M.Sabau, M.Ilca, Ana Izigian and Ileana Arsenescu. Dept.of Physiology, Faculty of Medicine, Tirgu-Mures, ROMANIA.

1. Stretch in normal Ringer: Decrease of stimulating threshold depends on stretch, hyperpolarization or depolarization. Up to a certain degree of stretch, increase in contraction amplitude(ACC), of the time to peak tension (TPT), of total contraction(-DC) and relaxation duration (RXD). Sometimes depolarization can trigger an own rhythmic centre, avoided by Ca-excess, which decreases the positive inotropic action of stretch, only with single but not with rhythmic stimulation. 2. In Ca-rich Ringer: Slight increase or decrease of resting (RP) and action (AP) potentials, increase of ACC; with rhythmic stimulation significant increase in TDC: increase of total myocardial Na. 3. In Ca-poor Ringer: generally reversed effects. 4. In Na-65 with rhythmic stimulation significant increase in TDC: Increase of total myocardial Na. 3. In Ca-poor Ringer: generally reversed effects. 4. In Na-rich Ringer: slight decrease of ACC, TDC and TDP. 5. In Na-poor Ringer: generally reversed above effects. 6. Inderal: Slight decrease of RP, AP and overshoot, significant decrease of ACC(phenomenon avoidable by Ca-excess but not by epinephrine). No relationship between electric and contractile phenomena. Inderal decreases significantly TDC and RXD in Na-poor Ringer, TDC and Ca-poor Ringer, and Ca-poor Ringer, and Ca-poor Ringer, and RDC in Na-pich Ringer. TDC in Ca-poor Ringer and RDX in Na-rich Ringer.

INTERPRETATION OF THE EFFECTS OF EXTERNAL K+ CONCENTRATION ON THE MEMBRANE POTENTIAL. P. Ascher. Lab. Neurophysiol. Cell., CNRS, 91, Gif sur Yvette, France.

An attempt has been made to define the membrane potential by taking into account both the passive (M_j) and active (M_j) fluxes of the main ionic species. If the membrane potential is stable, one can write $\sum M_j + \sum M_j = 0$ (eq. 1) $\sum M_{j} + \sum M_{j} = 0$ Solutions of this equation have been obtained by making three hypotheses. (1) The net

passive flux (M_i) for each ion follows the constant field equations (Goldman, 1943; Hodgkin and Katz, 1949). (2) The active flux of Na⁺ is a function of the external K⁺ concentration (N_o) and of the internal Na⁺ concentration (Na_i) such that $M^{i}_{Na} = M_{max} \left[\frac{K_{o}^{2}}{(K_{o}^{2} + K_{m}^{2})} \right] \cdot \left[\frac{Na_{i}^{3}}{(Na_{i}^{3} + K_{n}^{3})} \right]$

(3) The active fluxes of Na⁺ and K⁺ are coupled with a ratio 3/2 such that 2M_{Na} + 3M_K = 0. It will be shown that with these hypotheses, eq. 1 can account for two unexplained observations: the depolarizing effects of low K solutions (e.g., Gorman and Marmor, 1970) and the enhanced depolarizing effects of high K solutions when Na_i is above normal (Baylor and Nicholls, 1969). (Baylor, D.A. and Nicholls, J.G., J. Physiol., 1969, 203, 571; Goldman, D.E., J. gen. Physiol., 1943, 27, 37; Gorman, A.L.F. and Marmor, M.F., J. Physiol., 1970, 210, 897; Hodgkin, A.L. and Katz, B., J. Physiol., 1949, 108, 37)

CHANGES IN SACCADIC EYE MOVEMENTS PRODUCED BY CEREBELLAR CORTICAL LESIONS. <u>Jurgen C.</u>

Aschoff and <u>Bernard Cohen</u>. Department of Neurology, Mount Sinai School of Medicine, City
University of New York, New York, N.Y., U.S.A. 10029.

Spontaneous horizontal saccades of monkeys were changed by unilateral lesions of the cerebellar cortex. After ablation of parts of the vermis and adjacent paravermis including Larsell's lobules VI and VII, the eyes moved most often from the midposition into the contralateral hemifield of movement, and there were few saccades into the ipsilateral hemifield. In 4 of 6 animals with one-sided vermian and paravermian lesions, saccades to the contralateral side were larger than to the ipsilateral side after operation. In these monkeys the eyes tended to move from the midline to the opposite side in single saccades and return toward or past the midline in a series of smaller movements. Amplitude/velocity relationships of saccadic movements, slow pursuit movements, and optokinetic nystagmus were not much affected by the cerebellar cortical lesions. These data support the hypothesis that neural organizations in the cortex of the vermis and paravermis participate in producing gaze shifts or positions of fixation to the ipsilateral side.

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EVIDENCES THAT THE HEMODYNAMIC RESPONSE TO OSCILLATORY INPUTS INDUCED BY "SINUSCIDAL EXERCISE" IS MEDIATED BY THE SYMPATHETIC NERVOUS SYSTEM. E.Ashkar. Inst. of Physiology, Fac. of Medicine, Univ. of Buenos Aires and Natl. Council of Tech. and Sci. Res., Buenos Aires, Argentina.

Trained dogs with indwelling electromagnetic blood flow sensors performed exercise at sinus time-varying work loads to study the role of the autonomic nervous system in the dynamic adjustments of circulation. A sinusoidal generator was attached to a motor driven treadmill to control amplitude and frequency of speed modulations. Heart rate and mean acrtic blood flow were continuously recorded during repetitive trials at constant speed amplitude (2-10 km/hr peak to peak) and forcing frequencies between 0.02 and 0.2 Hz. Amplitude and mean level variation in cardiac output and heart rate were studied before and after propranolol, guanethidine and stropine administration. It was found that after sympathetic blocking, the amplitude variation and mean level of cardiac output and heart rate fluctuation were reduced. After parasympathetic inactivation, the amplitude variation of heart rate and cardiac output was maintained, whereas the mean level of fluctuation was elevated in the former and variable in the latter. Analysis of the amplitude data indicates that the sympathetic nervous system plays a major role in the dynamic adaptations of circulation.

MAGNESIUM AND CALCIUM FLUXES IN SINGLE MUSCLE FIBRES. C.C.Ashley and J.C.Ellory, Zoology Dept., Bristol Univ., and Inst. of Animal Physiology, Babraham, Cambridge, England.

The divalent cations Mg²⁺ and Ca²⁺, although important in regulating contraction behave in markedly different ways within muscle cells. Using ²⁸Mg injected axially into Balanus nubilus or Maia squinado single muscle fibres, the Mg efflux has been found to approximate to simple exponential kinetics, with a mean rate constant of 0.156 (S.E. ± 0.031) x 10⁻⁴ sec⁻¹ at 20-25°C. The internal diffusion coefficient for Mg was 2-4 x 10-7 sec⁻¹. From a total fibre Mg of 10-18 mmoles/kg wet weight, the Mg efflux was 6-12 pmoles/cm²/sec. In contrast the efflux of ⁴⁵Ca does not follow a simple exponential relationship and Ca is not freely diffusible inside the fibre. The Mg efflux was reversibly inhibited by 100mM MgCl₂ or CaCl₂, or lmM LaCl₃ salines applied externally, whilst Ca efflux was not markedly affected. Caffeine or KCl-induced contracture caused an increase in Ca efflux, whilst Mg efflux was unchanged. This increased Ca efflux was not affected by lmM LaCl₃ applied externally.

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70 ELECTROPHYSIOLOGICAL CORRELATES OF CONDITIONED REFLEX EXITATION AND INHIBITION. E.A. Asratyan. Inst. of Higher Nervous Activity and Neurophysiology, USSR Acad. Sci., Noscow, USSR.

When recording electrodes are exactly located on the cortical points of the animals paw, which performs a local motor conditioned reflex, the following phenomena are observed: In the course of the reflex elaboration in addition to the initial evoked potentials (ordinary, augmenting, recruiting etc) of this cortical point a late surface-negative potential develops. It is strictly localized and relatively stable: its fluctuations correlated exactly with the alterations of conditioned reflexes in their effector display. Correlation between its presence and positive conditioned reflex, as well as between its absence and reflex inhibition is clearly seen during well as between its absence and especially the elaboration of delayed conditioned reflexes. Once such a reflex is formed this potential is completely absent (or its latency substancially increases) at the inhibitory phase of the conditioned stimulus action, whereas at the excitatory phase of the same stimulus action the potential appears and increases (or its latency reduces).

71 INFLUENCE OF THE STOMACH ON THE PERISTALTIC ACTIVITY OF THE DUODENUM.

E. Atanassova. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia,
Bulgaria.

Chronic experiments were made on dogs with section of the stomach at the level of incisura angularis and subsequent restoration of the entirety of the stomach. Bipolar ball-shaped silver electrodes were implanted on the muscular walls of the stomach and the duodenum. By the character of the bioelectrical activities of the stomach and duodenum one could judge their mechanical activity. Unchanged rhythm is to be observed in the slow potentials from the wall of the stomach above the section and a delay in the rhythm of the appearance of the slow potentials from the segment of the stomach below the anastomosis. The spikepotentials, an expression of higher activity, appear in the rhythm of the delayed slow potentials in the stomach below the section. It was established that the duodenal spike activity is precisely correlated with the spike activity of the stomach segment below the anastomosis. This demonstrates the regulatory role played by the stomach in relation to the motor activity of the duodenum.

TRANSPORT AND METABOLISM OF CITRIC ACID CYCLE INTERMEDIATES IN HAMSTER SMALL INTESTINE. J. L. Atfield, P. A. Sanford & D. H. Smyth. Department of Physiology, The University, Sheffield, S10 2TN, England.

The ability of citric acid cycle intermediates to stimulate hexose

Direct measurement of the lung tissue resistance : a new method. G. Atlan, J.E. Lafosse, Ch. Jacquemin. Laboratory of Physiology - C.H.U. C.H.U. CRETEIL (94) - France.

When the gaseous flow is stopped by a mouth stopcok the overall mechanical lung effective power (rate of work of breathing (W_{L})) during a closed loop of compression of alveolar gas is entirely lost through the lung tissue resistance (R.).

Assuming a linear differential equation for the relation between the stress, i.e. the transpulmonary pressure (ΔP_{\parallel}) and the tissue strain, i.e. the tidal volume (V_{\parallel}), R_{\parallel} equals $W_{\parallel}/V_{\parallel}^{T}$ (Jacquemin and al. – J. de Physiol. 1967, 59, 435) V_{\parallel} being the thoracic effective strain rate. W_{\parallel} is the product of the respiratory frequency f by the work of breathing ΔP_{\parallel} dVT when a ventilatory cycle of the subject is following a sinusoIdal pattern, V_{\parallel} equals W_{\parallel} f V_{\parallel} . ΔP_{\parallel} is measured as the pressure difference between mouth and oesophagus, V_{\parallel} as the perithoracic tidal volume obtained with open volumetric body plethysmograph.

The magnitude of the volume of the compressed alveolar gas being 200 ml, (rate of breathing: 1-3 Hz) the lung tissue resistance, amounting 0.1-0.2 cm H_20 per liter per sec., is varying with amplitude and frequency.

The proposed method with a sinusoidal input, the principle of which is similar to the step-input method described by Varène and al. - (C.R. Soc. Biol., 1964, 3, 511) appears to be quite stisfactory: it gives specifically the tissue resistance per se and not, as usually, the difference between the measured total resistance with oesophagal balloon and the plethysmographically measured gaseous resistance.

CONDITIONED AND UNCONDITIONED RESPONSES DURING THE CONTINGENT NEGATIVE VARIATION. <u>E.Atsev, E.Dintcheva, D.Popivanov</u>. Res.Group on brain functions, Bulgarian Academy of Sciences, Sofia, Bulgaria.

In respect of studying some peculiarities of the brain functional state during Contingent Negative Variation (CNV) of healthy people, the authers have applied an additional electrocutane stimulus (S-3) in a pseu-do-random rate between click (S-1) and flash (S-2) of the Gr.Walters experiment. It was found that responses to a real electrocutane stimulus are better expressed during CNV, displaying certain peculiarities in dependence of their distance from the click. In the case of pseudo-random application of stimuli in 4 standard variations (S-3 just after S-1;S-3 in the middle between S-1 and S-2; only S-1 and S-2) the formation of conditioned responses in the time when S-3 should be given, was established. These responses show also characteristic peculiarities in dependence of their place in CNV.

The authers assume that the functional state of the brain during CNV provides conditions for facilitated formation of unconditioned and conditioned reactions. They have attempted to explain this from the viewpoint of the informatics and have looked for some application of their conceptions in the studying of the mental work capacity.

INFLUENCE DES FIBRES AFFERENTES VAGALES SUR L'ACTIVITE DU CORTEX CEREBRAL (AIRE SII). ENREGISTREMENT SIMULTANE DE LA DECHARGE DES NEURONES VAGAUX ET CORTICAUX. M. Aubert, N. Meī. C.N.R.S., I.N.P. (Dept. Neurophysiologie végétative) - 13 MARSEILLE - 9ème - France.

On sait qu'une partie au moins des fibres afférentes vagales se projettent sur le cortex cérébral. Le but de ce travail est d'étudier les modifications corticales produites par l'activation d'un petit nombre d'entre elles. Les deux microélectrodes extracellulaires utilisées pour cela sont placées, la première dans le ganglion plexiforme, et la seconde dans l'aire somato-sensorielle SII. L'activité électrique d'un neurone (ou d'un petit nombre de neurones) est recueillie dans le ganglion plexiforme à l'aide de la première microélectrode. On stimule ce (ou ces) neurone(s) au moyen de cette microélectrode et on observe les modifications corticales qui en résultent grâce à la seconde microélectrode. La stimulation vagale ainsi réalisée entraîne 1°) l'inhibition de certaines unités corticales spontanément actives; 2°) l'activation d'unités jusque-là silencieuses. Ces résultats démontrent que l'activation d'un nombre très réduit de fibres vagales est capable de modifier l'activité de l'écorce cérébrale.

76 CHLORIDE EXCHANGE ACROSS EHRLICH ASCITES TUMOR CELLS. F.Aull. Dept.of Physiol., New York Univ.Sch.of Med., N.Y., N.Y., U.S.A.

Measurements of the electrical potential difference across the ascites tumor cell membrane had shown that the cells depolarize in sulfate solutions, but not in nitrate solutions. Since it has been assumed that chloride is distributed passively across the cell membrane it was of interest to compare tributed passively across the cell membrane it was of interest to compare the chloride exchange in sulfate and nitrate media. Cells were equilibrated in chloride exchange in sulfate and nitrate media and the steady with either sulfate or nitrate. Radioactive chloride was added in the steady state to measure the efflux rate coefficient. Chloride turnover in sulfate and nitrate solutions differs strikingly. Whereas the efflux rate coefficient in initrate did not vary significantly from the control over a range of 181 to 16 mEg/liter (Cl)₀, in sulfate the efflux coefficient increased linearly with decreasing (Cl)₀. For example in sulfate containing 40 mEq/liter chloride the turnover of exchangeable cell chloride was 10 times faster than in control or nitrate media. However, steady state chloride influx decreased as (Cl)₀ was lowered in nitrate or sulfate. This is expected if chloride exchange is passive. Influx was always higher in sulfate than in nitrate at a given (Cl)₀. The nature of this increased chloride flux in sulfate solutions remains to be determined. Supported by USPHS Grant CA 10625.

77 MODULATION OF VISUAL INFORMATION BY SUPERIOR COLLICULUS ACTIVATION. F. Ayala,
A. Salgado and A. Fernández-Guardiola. Instituto de Investigaciones Biomédicas,
UNAM. México, D.F. México.

The conditioning electrical stimulation of the superior colliculus (CS) produces depression of the presynaptic component of the photic evoked responses in the Lateral Geniculate Body (LCB) and the appearance of a sharp second response to visual stimulation in the visual cortex and LCB. This second response has a latency of 80-120 msec. The unitary extracellular analysis of both structures showed neuronal discharges in LCB and VC during the development of the second photic response. The microelectrodes recording reveals that the second photic response in LCB corresponds to the activation of the same cells which are activated during the primary evoked response.

On the other hand, the CS conditioning activation provoked centrifugal effects on the Electroretinogram evidenced by the enhancement of the b2 scotopic component of the b wave. The latency analysis reveals that this modification of b2 coincides with the second photic response in LGB and VC.

78 SPECIES DIFFERENCES IN THE ANTICOAGULANT ACTIVITY OF AFLATOXIN. E.A.Bababunmi and O.Bassir. Dept. of Biochemistry, Ibadan University, Ibadan, Nigeria.

A study of the effects of aflatoxin B_1 (dose 58 ug/kg) and 4-hydroxycoumarin (dose 50 mg/kg) on blood clotting in eleven animal species has been made by following the thrombotest times. The results of the experiments indicated that there is a species variation in the anticoagulant activities of aflatoxin B_1 and 4-hydroxycoumarin. A relationship between the anticoagulant activities of these coumarin compounds and the nutritional status of each animal species is discussed.

MECHANISM OF SUPPRESSION OF VENTRICULAR PACEMAKERS ACTIVITY WITH HIGH-FREQUENCY EXCITATION. E.B. Babsky, S.K. Saidkarimov, L.S. Ulyaninsky. Inst. of Normal and Pathological Physiology, Moscow.

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Impulses from the sinoatrial node or electrical stimuli more frequent than the spontaneous frequency of ventricular pacemakers activity suppresses their automaticity. This results in a preautomatic pause when delivery of impulses to the ventricles stops. Experiments on an isolated rabbit heart with atrioventricular block show that cuabaim and monoiodacetate, dinitrophenol, potassium cyanide and sodium azide prolong preautomatic pause after stoppage of electrical stimulation of the ventricles. Perfusion of an isolated heart with ATP solutions and solutions with increased [K] or reduced [Na] shortens preautomatic pause. These effects are removed by blocking ATP-ase activity with cuabain. After heart poisoning with energy metabolism inhibitors ATP shortens prolonged preautomatic pause. The balance between active and passive ion transport in the ventricular pacemakers is possible only with low-frequency impulses. With arrival of frequent impulses from the sincatrial node or with frequent electrical stimulation of ventricles active ion transport proves insufficient, and generation of impulses by ventricular pacemakers stops temporarily. This is the cause of the preautomatic pause.

ADRENERGIC CONSTRICTION AND CHOLINERGIC DILATATION OF MUSCLE BLOOD VESSELS IN RESPONSE TO DIFFERENT EMOTIONAL STIMULI. G. Baccelli, G.D. Ellison, G. Mancia and A. Zanchetti. Cardiovascular Res. Inst., Univ. of Milan and Cardiovascular Res. Ctr., CNR, Milan, Italy.

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Muscle blood flow was recorded by means of electromagnetic probes from one or both hind limbs of ten unanaesthetized cats while exposed to several different stimuli having emotional significance for them: confrontation with a potentially aggressive cat, confrontation with a dog, presentation of a mouse or of food. All cats showed iliac vaso-constriction during the period of immobile reaction to an aggressive cat. The other stimuli, however, and particularly presentation of a dog, could elicit iliac vasodilatation instead, though the hind limbs remained immobile. Iliac vasodilatation was a less consistent response, and three of the cats reacted with vasoconstriction to all stimuli tested. Sympathetic mechanisms were responsible for both vasoconstriction and vasodilatation, as both responses disappeared in the sympathectomized limb. Vasoconstriction was mediated through adrenergic fibres as it was abolished by bretylium or guanethidine, while vasodilatation resulted from activation of sympathetic cholinergic fibres as it was prevented by intravenous or close intrarterial injection of methylatropine.

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MECHANISMS OF TONIC AND PHASIC CONSTRICTION OF MUSCLE BLOOD VESSELS DURING DESYNCHRONIZED SLEEP. G. Baccelli, G. Mancia and A. Zanchetti. Cardiovascular Research Inst., Univ. of Milan, and Cardiovascular Res. Ctr., CNR, Milan, Italy.

While desynchronized sleep is accompanied in cats by a vasodilatation diffuse to all visceral beds, muscle blood vessels show a tonic constriction phasically reinforced concomitantly to local twitches and REM bursts (Mancia, Baccelli, Adams, Zanchetti, Am. J. Physiol., 1971, in press). The mechanisms of this vasoconstriction have been investigated in cats carrying an electromagnetic flow probe around an external iliac artery, as well as an arterial cannula for monitoring blood pressure. The phasic waves of iliac vasoconstriction were not due to the mechanical effect of muscle twitches as were not prevented by a spinal transection at L4 sparing the sympathetic but not the somatic innervation of the hind limbs. Local sympathetic my demonstrated that phasic vasoconstriction was basically due to sympathetic activity. The mechanisms of the long lasting or tonic vasoconstriction appear to be more complex: among other factors, participation of a metabolic component (decreased production of vasodilating metabolites during the atonia of desynchronized sleep) is suggested by observations in cats spinalized at L4.

PRODUCTION AND BIOLOGICAL EFFECTS OF ERYTHROPOIETIN (E). I.Baciu, Rodica Daniello, T.Pavel, Mariana Deac. Dept.of Physiology. Inst.of Med. and Pharm. Cluj, România.

Authors have studied, in vitro, the release of erythropoietin (E) from erythrogenin (E-genin), an \(\)-globulin. Serum from anephric rats, containing this substance was incubated with renal erythropoietic factor (REF), prepared according to Gordon from hypoxic kidneys of rats. The release of E, caused by this factor, was compared with that produced by various other hydrolases. It was found that acetylcholinesterase and hyaluronidase produced a release of E from E-genin. The release of E in the absence of kidneys might be produced by activation of other enzymes that REF. E-genin is produced by the reticulo-endothelial system, since previous intravenous administration of colloidal carbon particles, was found to diminish the increase of serum erythropoietin and the erythrocytary response in rats exposed to hypoxia. E stimulates the function of hemopoietic bone marrow by activating the synthesis of nucleic acids, by enhancing the division of erythroid cells and by increasing blood supply to the bone marrow. Cyclic changes of radiosensibility in relation to the induced mitotic phases were noted. The primary effect of E is on the stem cell.

KINETICS OF GLUCOSE REABSORPTION IN PROXIMAL TUBULE OF THE RAT KIDNEY UNDER NORMAL AND ELEVATED PLASMA GLUCOSE CONCENTRATION.H.v.Baeyer, D.Haeberle and Ch.v.Conta.Inst. of Physiology, Univ. of Munich and Leibniz Rechenzentrum of the Bavarian Academy of Siences, Munich, West Germany.

Using microperfusion techniques, transport constants of glucose handling in the rat proximal tubule were measured. From these values, a concentration profile of glucose along the proximal tubule under free flow conditions can be calculated on the basis of the Gertz model of fluid reabsorption by integration of the following equatation: $\dot{v}(\text{de/ds}) + c(\text{d}\dot{v}/\text{ds}) = 2r\bar{v} \phi^{\text{gluc}}$; At normal plasma glucose concentration (Pg), there is a good coincidence with reported data(Rohde et al.1968). At higher Pg, glucose reabsorption is time dependent. After Pg elevation glucose concentration at first decreases along the proximal tubule. With infusions longer than 40 min.end proximal glucose concentration remains constant, or even tends to increase relative to Pg. This is not to explain by passive backdiffusion alone. We assume, that glucose concentration at the intracellular transport sites is increased to such an extent, that a carrier mediated backtransport occurs. Measurement of glucose influx under phloridzin inhibition favors this hypothesis.

IONIC STRENGTH AND PH EFFECTS ON MECHANICAL PROPERTIES OF A GLYCEROL EXTRACTED CATCH MUSCLE (ABRM). F. Baguet and S. Sleewagen. Dept de Physiologie. Univ. de Louvain, Louvain, Belgium.

Glycerol extracted ABRM are suspended in ATP-saltsolution in presence of graded increase of ionized calcium concentration using calcium-EGTA buffers at pH 7.0 (20°C). Peak tension developed from 10^{-8} to 10^{-4} M Ca^{++} , increases according to a sigmoide shape curve. When ionic strength increases with increasing KCl concentration (30, 65, 150 and 250 mM), the relationship does not change but the ability to develop tension at a same calcium ionconcentration is much higher. Moreover, fibres contracted at low ionic strength (10^{-4} M Ca^{++} , 30 mM KCl) are able to develop more tension (about 50 % of previous level) by changing the contractile solution for another containing less calcium ions (5 10^{-7} M) but more KCl (150 mM). Contracted fibres relax at low ionized calcium concentration ($<10^{-8}$ M); relaxation is slow and incomplete at low ionic strength (30 mM KCl), rapid and nearly complete at high ionic strength (150 or 250 mM KCl). Using acid contracting solutions (pH 6.5) much less tension is developed at any KCl concentration and the relaxing solution is no more efficient especially at low ionic strength. Low ionic strength and acid pH give rise to the catch, the maintenance of which is not controled by the level of ionized calcium concentration.

FEEDING EFFECTS OF HYPOTHALAMIC INJECTIONS OF PROSTAGLANDINS. C. A. Baile and S. M. Bean. Dept. of Nutrition, Harvard School of Public Health, Boston, Mass. 02115 USA. C. W. Simpson and H. L. Jacobs. U.S. Army Lab., Natick, Mass. 01760 USA.

Prostaglandins (PG) which are ubiquitous and can affect many physiological functions, decrease food intake of rats when injected sc. To determine if PG can act directly on the CNS, 225-275 g male rats were prepared with bilateral cannulas in the ventromedial (VMH), perifornical (PFH), anterior (AH), or lateral (LH) hypothalamic areas. 1 Al of saline (.9%) was injected bilaterally prior to a daily 2-hr feeding on days 1 and 4. 1 Ag of PG in 1 Al saline was injected on day 2. No injection was given on day 3. PGE injection into the PFH decreased food intake in comparison with two saline injections by 36, 25, 18 and 15% (p<.01) after 15, 30, 60 and 90 min, respectively. After 120 min food intake had recovered to within 6% of saline. VMH injections were nearly as effective in were no other apparent behavioral effects—H₂0 intake was normal and PGE injections caused no body temperature changes. PGB injections had much less effect than PGE Unilateral injections of 1 Al of PGE solution into VMH in doses of 1, 2, 4 and 8 Ag/Al decreased feeding by 15, 55, 80 and 85%, respectively. Because of the interrelationship of PG, fatty acids and adipose tissue, and because PG depress food intake by acting on the CNS, PG may have a role as intermediaries between fat depots and hypothalamic energy balance regulation.

CELLULAR AND BIOCHEMICAL SWITCH-OVER MECHANISMS IN THE SMALL INTESTINE OF NEWBORN MAMMALS. K.Baintner, jr.-B. Veress. Dept. of Physiology, Res. Inst. for Animal Breeding, and II. Inst. of Pathology, Univ. Medical School, Budapest, Hungary.

The luminal side of the small intestine is lined by cells of the foetal type in the newborn and suckling age, respectively. These foetal cells contain a specialized organellum capable of absorbing undigested protein macromolecules. When this special capacity is lost /"closure"/, the foetal type cells are replaced by a new type in the course of the continuous re-

matromotecutes. When this special capacity is lost / closure /, the roetal type cells are replaced by a new type in the course of the continuous regeneration process of the intestinal epithelium.

Independently from this exchange of cell type, milk, the natural food during the suckling age exerts a certain controlling action on the intestinal digestive processes. The colostrum of species of the non-selective protein absorption type contains a considerable amount of trypsin inhibitor which completely inhibits intestinal proteolysis during the first days of life. Intestinal protein digestion and amino acid absorption can not start until the colostrum begins to transform to normal milk which involves a considerable reduction of its trypsin inhibitor content. The change of the cell type and the switch-over of digestion are not always coincident. Sometimes the proteins undergo digestion prior to reaching the absorbing cells. This phenomenon is called virtual closure.

EFFECT OF VASOPRESSIN ON DISTRIBUTION OF GALACTOSE IN EVISCERATED - NEPHRECTOMIZED DOG. A. Baisset, L. Dang-Tran and P. Montastruc, Lab. of Applied Physiology, Faculty of Medicine, Toulouse, France.

For verify the hypoglycaemic effect of vasopressin and for study the influence of this neurohypophyseal-peptide on membrane permeability to glucose, the authors have injected intravenously galactose (1 mg/kg) in eviscerated-nephrec tomized dog. Lysine-vasopressin infused during 180-240 minutes, at the total dosis of 50 to 300 mU, lowers the blood level of galactose. Small dosis of lysine-vasopressin renforces the effect of same direction of small quantities of insulin and reciprocally. The implication of this finding is that vasopressin, like insulin, causes the intra-cellular penetration of sugar that is not phosphorylated or otherwise utilized in the hepatectomized animals. This results seems to support the idea that vasopressin, like insulin promotes penetration of glucose and other sugars into muscle and fat.

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88 EEG ANALYSIS OF CORTICO-SUBCORFICAL FOCI IN THE TRANSFORMATION OF CONDITIONED REFLEXES OF VARIOUS BIOLOGICAL MODALITIES. M.V.Bajić, Dpt. of Physiology, Med. Col., University of Novi Sad, Yugoslavia, Europa.

The functional system of the conditioned reflex reaction of a certain biological modality is formed from dynamically mobilized structures of the whole organism, in which the CNS and the final result of functioning, i.e. actions, play a fundamental physiological role (I.P.Pavlov,1916;A.I. i.e. actions, play a fundamental physiological role (I.P.Pavlov,1916;A.I. i.m. actions, play a fundamental physiological structures of transformation of the conditioned defensive reflex into alimentary reflex, after the stage of inhibition, the inhibited EEG activity is reestablished, and it is only after this that EEG signals occur which indicate a shft to the new signal meaning of the conditioned stimulus. In the transformation of the alimentary reflex into the defensive reflex, already the first reinforcements of the reflex produced an EEG picture of redy the first reinforcements of the reflex produced an EEG picture of the conditioned defensive reflex; all of which indicates the primacy of the biological modality of the conditioned stimulus over the sensory modality.

89 INTRACELLULAR PRESSURE OF NITELIA IN VERY HYPERTONIC SOLUTIONS. H. Baker. American Red Cross Blood Research Laboratory, 9312 Old Georgetown Rd., Bethesda, Md. 20014, U.S.A.

Meryman (1) has demonstrated that dehydration by exposure to hypertonic solutions shrinks cells to a minimum tolerated volume, below which damage occurs to the plasma membrane. It has been proposed that this damage is membrane rupture due to a progressively increasing mechanical stress that arises from a resistance to membrane collapse. A mechanical resistance to collapse should generate a measurable pressure gradient across the cell membrane. Such a pressure is also implied by published thermal analysis experiments. Pressure measurements were made with miniature, air-filled, glass capillary manometers (0.015 mm diam. and 3 mm long). The open end was pushed into a 10-20 mm long internodal cell of Nitella axillaris and compression of the air bubble was measured microscopically with a graduated reticle. In a preliminary series, the Nitella yielded turgor pressures as high as 7 atm when bathed in "pond water" of less than 0.0005 osmolal, and this pressure dropped linearly with increasing osmotic potential until plasmolysis developed. The sensitivity of the above type of manometer (±0.01 atm) was insufficient to detect the predicted pressure gradient, even though the series of hypertonic sucrose solutions extended above the lethal concentration. A more sensitive technique is in development. (1) Meryman, H.T. in The Frozen Cell (G.E.W. Wolstenholme and M. 0'Connor, eds.) pp. 51-64. J.&A. Churchill, London, 1970.

SLOW AND FAST PHASE NYSTAGMUS OF VESTIBULAR ORIGIN AS STUDIED BY INTRACELLULAR RECORDINGS IN TROCHLEAR MOTONEURONS.

Biophysics, Univ. of Iowa, Iowa City 52240, U.S.A., and Laboratoire de Physiologie du Travail du C.N.R.S., Paris 5, FRANCE.

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In encéphale isole cats, acute lesion of the vestibular nerve produces spontaneous nystagmus with the slow component directed toward the lesioned side. Intracellular recordings from trochlear motoneurons (TMn's) show slowly rising depolarizations (slow phase)
interrupted by abrupt hyperpolarizations (fast phase) occurring with a period of about 400
msec. A totally different nystagmic mechanism is elicited by a brief electrical stimulation of the labyrinth on the lesioned side. In this case, a succession of sudden intense
membrane depolarizations are recorded in TMn's. Each burst has a duration less than 100
msec (fast phase) and is followed by gradual membrane hyperpolarization (slow phase). The
frequency and duration of the nystagmic bursts could be driven by labyrinth stimulation.
The injection of polarizing current and ions from the microelectrode demonstrates both
depolarizations to be EFSPs. Active nystagmic modulation of the TMn, during the slow and
fast phase, is thereby generated from two characteristic patterns of EFSPs in the TMn,
each terminated mainly by a disfacilitation and in some cases combined with an added IPSP
component. It is concluded that nystagmus is not produced at the level of the trochlear
nucleus, but represents motoneuronal recruitment by an intermittent and highly synchronous
presynaptic barrage whose origin resides in the vestibular complex of the brain stem.

SELECTIVE EFFECTS OF MUCOSAL AND SEROSAL ANAEROBIOSIS ON INTESTINAL ELECTRICAL ACTIVITY AND SUGAR TRANSPORT. R. David Baker and Malcolm J. Wall. University of Texas Medical

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Potential difference (PD) and short-circuit current (I_{sc}) were measured across sheets of rat and hamster jejunum. Without actively transported organic solute, PD and I_{sc} were far more dependent upon oxygen in the serosal solution than in the mucosal solution. On the other hand, the electrical response to D-galactose and to taurocholate were more sensitive to mucosal anaerobiosis than to serosal anaerobiosis. Uphill transport of an actively transported sugar was also far more dependent upon mucosal O_2 than upon serosal O_2 . Sugar transport and the electrical responses to sugars and to taurocholate require oxidative metabolism, but from a different source than the one supporting PD and I_{sc} in the absence of organic solute. Experiments with oxygen electrodes in sealed chambers showed that O_2 cannot diffuse all the way across the tissue from either side; it is apparently used by the tissue as rapidly as it can diffuse in. It is probable that mitochondria located farthest from the source of O_2 are not adequately supplied. Supported by USPHS Grant AM-05778

SKIN-GRAFTING AND BEHAVIOR IN THE FROG. R.E. Baker. Max-Planck Inst. of Psychiatrie, Munich, Germany.

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A variety of skin grafts were made in tadpoles of Rana pipiens at different stages of larval development. During metamorphosis, normal reflex activity developed in all animals, only to be replaced in some skingrafted frogs with misdirected reflexes. These responses were atypical for the host area but normal for the area of graft origin. The area of skin from which these misdirected responses could be elicited gradually spread over most of the graft. The position of the graft and its size determined whether misdirected reflexes would be given in the adult frog. At least 40 mm of skin had to be transplanted from back to belly or vise versa, and the graft had to be located across a reflexogenous zone boundary. Cutaneous receptive fields were mapped in normal control and skingrafted tadpoles and frogs, before, during and after metamorphosis. No changes in receptive field size or shape could be detected at any time during development or during the period of replacement of normal with misdirected reflexes. Receptive fields did not cross the graft boundaries to innervate the surrounding normal skin, or from normal skir onto the graft. It was concluded that misdirected reflexes were not the result of selective regrowth of peripheral nerves but were due to changes in the CNS after the sensory nerves had made contact with the skin graft.

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ELECTROPHYSIOLOGICAL STUDY OF PROJECTIONS OF SOMATIC AND VISCERAL SEMSO-RY PATHWAYS TO THE HYPOTHALAMUS. O.G. Baklavadjian, A.G. Arakelian, E.G. Ast-vazatrian. Inst. of Physiology, Armenian Academy of Sciences, Erevan, USSR.

The evoked potentials in the hypothalamus to stimulation of sciencia, splanchnic or vagus /cervical portion/ nerve in most experiments are characterized by short-latency responses with initial positive wave in the supramammillary and the postero-lateral and long-latency responses in all the other regions of the hypothalamus. In the focus of maximal activity unit discharge appears only on the descending phase of the focal potential. There is a great similarity in the distribution and the properties of somatic and visceral evoked potentials. Responses to acoustic and photic stimulation are more diffuse and the highly stable short-latency photic evoked potentials in the ventral part of the anterior hypothalamus are the result of a physical spreading of activity from the region of the specific optic pathways. It was found a high degree of convergence on single units of the posterior as well as the anterior hypothalamus. As a conclusion the evoked responses of the hypothalamic neurons activated by acoustic, photic, sciatic and visceral nerves stimulation have the characteristic of a secondary type response.

THE ROLE OF THE AMYGDALOID COMPLEX IN THE REGULATION OF ALIMENTARY BEHAVIOUR IN DOGS. A.N.Bakuradze, A.V.Asatiani, M.G.Dateshidze, T.M.Nikolaeva, N.A.Salukvadze. Department of Physiology, Tbilisi Medical Institute, Tbilisi, USSR.

Experimental intervention (stimulation, lesion) involving the corticomedial group of nuclei of the amygdaloid complex produces characteristic changes in the alimentary behaviour of dogs and in the secretory and motor activity of the main digestive organs; stimulation causing sniffing, licking, increase in the secretion of saliva and gastric sniffing, licking, increase in the secretion of saliva and gastric juice, elevation of the biliary bladder tone, inhibition of the periodic motor activity of the stomach, etc. While bilateral lesion of this group of the amygdala brings about an acute depression of the condigroup of the amygdala brings about an acute depression, "oral tendency", tioned alimentary reflexes, alimentary perversion, "oral tendency", etc. Stimulation or lesion of other amygdaloid nuclei appears not to produce such changes in the alimentary behaviour of the animal.

95 CONDITIONED INSULIN AND GLUCAGON FOOD INTAKE. Saul Balagura.
Dept. of Psychology, University of Chicago, Chicago, Illinois, USA.

Previous research carried out in my laboratory showed that it is possible to condition insulin hypoglycemia and a corresponding increase in food intake in albino rats. It was also demonstrated that the hyperglycemia that follows glucagon injections can also be conditioned. We have now recorded, for the first time, the time parameters of the glucagon action on feeding behavior, and have demonstrated that it is possible to condition the delay of eating induced by glucagon injections, using an isotonic saline injection as the conditional stimulus. The results are explained in terms of a neuroendocrine model in which endogenous insulin or glucagon are released following presentation of the conditional stimulus. (This research was supported by United States NIH grant No. MH-14596.)

INTRAREMAL PRESSURE GRADIENTS IN EXPERIMENTAL REMAL FAILURE. P.Bálint, A.Fekete, E.Szőcs. Inst. of Physiology, Med. Univ., Budapest, Hungary

Acute renal failure was induced in dogs by intravenous application of mercuric chloride or by temporary occlusion of the renal artery. Azotaemia developped. The following parameters of renal function were determined: renal blood flow (venous effluent), glomerular filtration rate, arterial, intrarenal deep venous and renal venous pressures; glomerular capillary pressure was considered to equal stop flow ureter pressure plus colloid osmotic pressure of plasma proteins. Series connected renal resistances were calculated by dividing the corresponding pressure differences by renal blood flow. Whereas arterial, deep venous and renal venous pressure are about the same under control conditions and in renal failure, glomerular capillary pressure is significantly less in the latter conditions. Overall renal resistance is either unchanged or slightly decreased. There is, however, a disproportionate decrease in postglomerular resistance with a componsatory increase in preglomerular resistance. The pronounced decrease in glomerular filtration with maintained arterial pressure and renal blood flow can be explained on the basis of the alterations of intrarenal vascular resistances.

THE ROLE OF CERTAIN ENCYMES IN HONOVALENT CATION TRANSPORT. B. Ballantyne. Medical Division, Chemical Defence Establishment, Porton Down, Salisbury, Wiltshire, Great Britain.

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Using the avian masal gland as a biological model, the roles of certain enzymes in the transport of sodium and potassium ions has been investigated by biochemical and histochemical methods. Both ouabain-sensitive and ouabain-insensitive adenosine triphosphatases increased markedly following the onset of secretory activity. Their roles and functional inter-relationships will be discussed. Although a basic role for acetylcholinesterase could not be demonstrated, other than its function in the cholinergic innervation of the gland, a clear relationship between monovalent cation transport and butyrylcholinesterase activity in the secretory epithelium was found. It is proposed that the function of butyrylcholinesterase is to modify the lipid permeability characteristics of the cell membrane for the transport of monovalent cations. Elevated concentrations of β -glucuronidase in the secretory cells were found after the onset of secretion. The possible role of β -glucuronidase in nasal gland function by hydrolyzing glucuronide conjugates of glucocorticoids and facilitating the concentration of aglycon in the tissue will be discussed, although there may be a more fundamental function for the enzyme in membrane transport mechanisms.

REGIONAL DIFFERENCES IN THE AUTONOMIC REGULATION OF BLOOD FLOW AND METABOLISM IN ADIPOSE TISSUE. K.Ballard and S.Rosell. Cardiovascular Res. Lab., Univ. of Southern Calif., Los Angeles, Calif., U.S.A. and Dept. of Pharmacology, Karolinska Inst., Stockholm, Sweden.

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Adrenergic neuro-humoral influences on vascular and metabolic responses were studied in autoperfused canine subcutaneous, omental and mesenteric adipose tissue. Resting blood flow was the same in all three tissues (8-12 ml/min/100g). Continuous electrical excitation (1-9/sec for 30 min) of the nerve to subcutaneous or omental tissue caused a) vasoconstrictim accompanied by reduced regional blood volume and b) increased output of glycerol and free fatty acids. The capacity for fluid filtration (capillary filtration coefficient, CFC) increased. The clearance rate of $^{125}\mathrm{T}^-$ was reduced despite constant blood flow. Resting CFC (0.05 ml/min/mm Hg/100g) in omentum was twice as high as in subcutaneous tissue. In omentum, constriction often reverted to dilatation and regional blood volume gradually returned to resting level despite continued stimulation. The mesenteric tissue exhibited no or weak vascular and metabolic responses to nerve stimulation. Close intra-arterial infusion of noradrenaline (0.001-0.01/pg/ml plasma for 30 min) caused similar vascular responses but lipolysis was enhanced only at high plasma levels of added catecholamine. It is concluded that a) vascular and metabolic responses to sympathico-adrenal activity are not uniform in adipose tissue from different regions in the same animal, b) circulating catecholamines may be less important for lipolysis than the outflow from nerves and c) in some adipose tissue, regulating factors other than those of autonomic origin must predominate.

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MICROVASCULAR HYPERSENSITIVITY IN ESSENTIAL HYPERTENSION AS PRIME PATHOGENETIC AETIOLOGY THEREOF, AND AS COMMON DENOMINATOR OF ALL KINDS OF HYPERTENSION. T.A. Balourdas, Howard University Medical School, Washington, D. C., U.S.A.

The unknown pathogenesis of Essential Hypertension is being a great unsolved scientific and social problem in Biomedicine. To elucidate this puzzling problem investigations were undertaken pertaining to the microcirculatory changes in the mesoappendiceal microvessels of the spontaneously hypertensive rats (NIH breed of Japanese origin), using the mesocaecum bioassay preparation for direct visualization of the capillary pattern via biomicroscopy. Results. In all in vivo 12 experiments the capillary pattern was excellent without exhibiting any structural lesion. The microvascular hypersensitivity evidenced by the Epinephrine threshold test on the arteriolar-precapillary sphincters was found very high from the average normal 1:4X10-6 up to 1:0.2X10-9 and 1:0.1X10-9 E.T.C. The finding is indicative of vascular hypersensitivity. The hypersensitive microvessels become hyperreactive to endogenous or exogenous vasoactive angiotropic agents as Catecholamines, steroids, polypeptides, etc., hence permanent generalized vasoconstriction and hypertension. In the same twelve hypertensive animals we found "retinal microvascular hypersensitivity" (Circulation, XLII: 111-133, 1970 (Oct). The "Microvascular Hypersensitivity and Microvangiopathy Theory", inferred from our exper. studies, and explaining many morbid entities in Biomedicine, was reported (Balourdas, T.A., IV Internat. Congress of Pharmacology, 7/'69, Basel, Switzerland, & Fed. Proc., 28:682, 1967). The results indicate that the multicausal vasc. hypersensitivity-hyperreactivity (hereditary, acquired) might be the pathogenetic aetiology of essential hypertension and the denominator of all forms of Hypertension.

100 LIPIDO-PROTIDIC FRACTIONS RATIO IN ATHEROSCLEROSIS. N.Baltă, S.Căpâlnă, N.Drăgulescu, Al.Ciplea. Inst.of Normal and Pathologic Physiology,

Some metabolic lipido-protidic disorders preceding functional and structural changes of arterial wall has been generally accepted.Qualitative and quantitative changes of phospholipids,triglycerids,cholesterol,betalipoproteins and protein fractions obtained by electrophoresis also,show a large teins and protein fractions obtained by electrophoresis also,show a large interdependence of them.Nevertheless,up to the present,afew studies investigated the ratio of plasma lipid and protidic fractions and the ratio of summary fractions in the two groups. This is the purpose of our investigation. Significant value for the diagnosis of atherosclerosis has the ratio phospholipids: total lipids, the ratio alfa_globulins: serumalbumins, and phospholipids: total lipids, the ratio alfa_globulins: serumalbumins to total litheratio betaglobulins: serumalbumins. The ratio phospholipids: total litheratio betaglobulins: serumalbumins and 0.148 in atherosclerotic femapids is 0.128 in atherosclerotic males, and 0.148 in atherosclerotic femaples. In comparing, the ratio is 0.98 in obesity and 0.223 in healthy mem. The most reduced values are in coronary forms, followed by atherosclerosis of peripherical arteries. Very high levels has been found in cerebral atherosclerosis. Alfa_globulins: serumalbumins ratio is 0.29 in atherosclerotic sclerosis. Alfa_globulins: serumalbumins ratio betaglobulins: serumalbumins is, generally, increased in atherosclerosis.

HYPERPNEA FOLLOWING ACUTE CORONARY OCCLUSION IN DOGS. C.M. Banerjee, P. Freedberg,
D.A. DeBias and M.H.F. Friedman. Department of Physiology, Jefferson Medical College,
Philadelphia, Pa., U.S.A.

The immediate cardiopulmonary effects following acute myocardial infarction were investigated in 18 mongrel dogs. The dogs were anesthetized with IV Pentobarbitol (30 mg/Kg) and non-fatal myocardial infarctions were produced by using a modified closed-chest technique (Fed. Proc. 29:841, 1970). In this method, small amounts of polystyrene beads (approximately 400 microns in diameter) were introduced into the coronary arteries during coronary angiography. Respiration and heart rates, EKG, arterial blood gas tensions and systemic blood pressure values were monitored during and following the procedure. The immediate post-infarction results show hypernea, systemic hypotension and hyperventilation (arterial hypocapnia and hyperoxia). There were no significant changes in heart rates within thirty minutes post-infarction period. The mechanism of marked hyperpnea is possibly a reflex phenomenon. We conclude that hyperpnea is one of the earliest diagnostic signs of acute myocardial infarction. The value of routine oxygen therapy following acute myocardial infarction appears uncertain.

(Supported by USPHS Grant HGRS 1969-01)

MECHANISMS OF DEPRESSED SWEAT GLAND ACTIVITY DURING ARTERIAL OCCLUSION. M. R. Banerjee, Dept. of Anatomy and Physiology, Indiana Univ., Bloomington, Indiana, USA.

The mechanisms of decreased thermal sweating activity during prolonged arterial

occlusion were investigated. Stimuli known to increase the sudomotor nerve impulse traffic were ineffective in increasing sweating in ischemic areas. Sweat glands remained responsive to parasympathomimetic agents but were unresponsive to local heating which presumably involved neuroglandular transmission. The suppression of sweating during arterial occlusion was found similar to neuroglandular junction blockade produced by Hemicholinium-3. Thus, the depression of thermal sweating in ischemia appeared to be associated with a decreased availability of the transmitter substance at the neuroglandular junction. In a cold room when the sweat glands of non-sweating subjects were stimulated by a cholinergic agent, arterial occlusion proximal to the sweating area promptly decreased the sweat rate and restoration of the blood supply immediately returned the sweat rate to the control level. Similar results were obtained in a warm room with sweat glands at a higher temperature when the initial non-sweating condition was produced by regional xylocaine anesthesia. Thus the depressed sweating activity could also be due to a reduction in the sensitivity of the sweat glands to the transmitter substance. However, local administration of a cholinergic agent at different times during the arterial occlusion period produced no reduction in the response of the sweat glands. These results are paradoxical but suggest that there may be several mechanisms involved in ischemic depression of sweating.

THE ACTION OF p-CHOROPHENYLALANINE AND RESERVINE ON THE ANALGESIC EFFECT OF MEPERIDINE IN RATS. B.Banić and M.Medaković. Dept.of Pharmacology, Faculty of Medicine, Univ. of Novi Sad, Novi Sad, Yugoslavia.

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Reservine, a nonselective depletor of 5-hydroxytryptamine (5-HT) is known to abolish the analgesic effect of morphine in rats. In previous known to abolish the analgesic effect of morphine in rats. In previous experiments p-chlorophenylalanine (p-CPA), a selective depletor of 5-HT, has been shown to prevent this inhibiting effect of reserpine. The action of rescrpine and p-CPA on the effect of meperidine has been studied (by the tail flick method) in rats in the present experiments. The analgesic effect of meperidine (15 mg/kg) was found to be partially antagonized in rats treated with reserpine (1 mg/kg) 3 hours before meperidine. The difference between the effect of meperidine in reserpine treated and untreated rats was statistically significant (p 0.005). In other rats p-CPA (300 mg/kg) was injected 2 or 4 days and reserpine 3 hours prior to meperidine. The effect of meperidine in p-CPA and reserpine treated rats did not differ significantly from the control effect of meperidine in did not differ significantly from the control effect of meperidine in untreated rats. These findings are comparable with the previous findings on the interaction between p-CPA, reserpine and morphine.

INFLUENCE OF NATRIURETIC AGENTS AND BLOOD PRESSURE ON COMPARTMENTATION OF

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RENAL BLOOD FLOW. R.O. Banks & E.C. Foulkes, Depts. Env. Health & Physiol. Univ. of Cincinnati Col. of Med., Cincinnati, Ohio 45219, U.S.A. We have previously shown that saline infusions in dogs result in post-glomerular shifts of plasma flow away from PAH-extracting regions (Fed. Proc. 1971 in press). These conclusions were best for the process of Proc. 1971 in press). These conclusions were based on 1) a modified Il31-serum albumin (RISA) washout technique, 2) measurement of PAH extraction and 3) distribution of Yb169-microspheres within the cortex. Similar reand 3) distribution of Yb109-microspheres within the cortex. Similar results have now been obtained with 5% mannitol (in 0.15 M NaCl) infused at 0.3 ml/min/kg for 30 min, furosemide (2 mg/kg) or unilateral infusions of 80 µmoles/min acetyl choline (ACH). All 3 procedures shifted flow from the PAH-extracting RISA compt. 1+2 (non-PAH-extracting). However, no consistent shifts of glomerular perfusion between outer, middle and juxta medullary cortices were observed with the microsphere technique following mannitol or furosemide. These data suggest that diversion of flow from RISA compt. 1+2 with these procedures is also postglomerular. Compts. 3 & 4 which presumably include inner medullary flow remained unaffected by saline mannitol ably include inner medullary flow remained unaffected by saline, mannitol, ACH or furosemide. Further we could observe no clear-cut dependence of flow through these compartments on BP over the range 40-160 mm Hg, indicating the possibility of medullary autoregulation. (Supported by NIH grants HE 10346 and 5P10 ES00159).

OBSERVATIONS ON THE ENTRY OF AMINO ACIDS INTO THE BRAIN OF THE RAT IN VIVO . Guadalupe Banos, P.M. Daniel, S.R. Moorhouse, O.E. Pratt. Dept. of Neuropathology, Inst. of Psychiatry, Univ. of London, England.

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Selective transport mechanisms carry some 20 amino acids into the cerebral cells at rates which increase with the blood concentration. The differences in rates of entry are wider than the differences in blood concentration, being high for nutritionally essential and a few non-essential amino acids, but very low for amino acids not found in protein or not normally present in blood. Most amino acids enter the brain more rapidly in the immediate postnatal period than later in life. The entry rates into the brain seem to be related to its needs for protein synthesis, being high at the time of maximum growth or protein formation but low for amino acids which can be readily made by cerebral cells or are not required for protein synthesis. That selective transport processes are present soon after birth is shown by the wide differences in entry rates of amino acids which are found at this time. Raising the blood concentration of one amino acid reduces the rate of entry of other amino acids into the brain which shows that a number of amino acids share common transport mechanisms of limited capacity.

The work was supported by the Nuffield Foundation, the Research Fund of the Maudsley Hospital, and Roche Products.

CHANGES IN THE LEVEL OF ACID PHOSPHATASE, BETA GLUCURONIDASE AND LEUCINE AMINOPEPTIDASE

ON THE PLASMA FOLLOWING OCCLUSION OF VARIOUS ABDOMINAL ARTERIES. T. Barankay,

IN THE PLASMA FOLLOWING OCCLUSION OF VARIOUS ABDOMINAL ARTERIES.

G. Horpácsy, M. Gergely and G. Petri. Institute of Experimental Surgery, University

Medical School, Szeged, Hungary.

The lysosomal labilization caused by tissue hypoxia has been studied by numerous investigators but at present relatively little is known about the sites in the body which are specifically responsible for releasing lysosomal enzymes. Changes in the activity of acid phosphatase, beta glucuronidase and leucine aminopeptidase /LAP/ in activity of acid phosphatase, beta glucuronidase and leucine aminopeptidase /LAP/ in the plasma caused by occlusion of either the celiac or superior mesenteric arteries or clamping of abdominal acrta were investigated. There was no difference in acid or by a superior mesenteric arteries. There was no difference in acid or clamping of abdominal arteries. The activity of LAP in plasma increased only after the various abdominal arteries. The activity of LAP in plasma increased only after the occlusion of the main splanchnic arteries. These findings suggest that the increase in plasma acid phosphatase and beta glucuronidase activity caused by shock may not be the result of splanchnic hypoxia only but the enzymes may be released from other tissues result of splanchnic hypoxia only but the enzymes may be released from other tissues somel enzymes in the plasma should be judged by the observation of more than one enzyme because the level of each enzyme may be altered by a cortain stimulus in a different way.

MINIMAL TIME OF TRANSMISSION OF INFORMATION THROUGH THE PRIMATE VISUAL SYSTEM. N. H. Barmack. Lab. of Neurophysiology, Good Samaritan Hospital, Portland, Oregon, USA.

The amplitude and latency of saccadic eye movements evoked by visual targets were measured photoelectrically in two monkeys (Macaca nemestrina) previously taught to track the targets. Targets with an instantaneous onset, traveling horizontally across a 50° tangent screen with a constant velocity of 130°/sec, evoke 14-16° horizontal saccades with a 125-190 msec range of latencies. Targets traveling with a constant velocity of 40°/sec evoke 2-7° saccades with a 135-200 msec range of latencies. The minimal time for the initiation of a saccade in response to a visual stimulus is 125 msec. Visual targets composed of two constant velocity segments were presented to the monkeys. The time of the instantaneous transition in target velocity was varied between 10-120 msec, and the effects of this change on saccadic amplitude and latency were measured. Saccadic amplitude but not saccadic latency was modified by decreases or increases in target velocity introduced during the first 90 msec of target movement. The modification of saccadic amplitude depended on when the velocity of the target was changed; the earlier in the trial the change was introduced, the greater was the modification. A change in the velocity of the target could alter the size of a saccade occurring only 50-70 msec later. These results indicate that visual information may modify an eye movement with a minimal time of one-half that necessary to initiate an eye movement.

INCREASE OF ALPHA RHYTHM IN ELECTROENCEPHALOGRAM OF SCHIZOPHRENICS AFTER EYE CLOSING AND DURING HYPERVENTILATION. T. C. Barnes, I. M. Gerson and J. Siverson. Philadelphia State Hospital, Pennsylvania 19114, U.S.A.

The electroencephalogram of schizophrenics has not shown characteristic features. We have found evidence of hidden or suppressed alpha in schizophrenics. In 160 schizophrenic patients 49 showed rebound of alpha after opening and closing eyes (percent time alpha was greater after eye opening and closing than before eye opening). In 156 non-schizophrenic State Hospital patients only 16 showed this alpha rebound. This difference is statistically significant with a P value less than 0.01. In 160 schizophrenics 35 showed increased percent time alpha during hyperventilation. In 156 non-schizophrenics only 16 had increase in alpha in hyperventilation. The P value is less than 0.01. We conclude that schizophrenics tend to have a partially suppressed alpha which supports the theory of Goldstein and Pfeiffer that the brain of these patients is in a state of arousal.

AN EXTREMELY FAST Pt - ELEKTRODE FOR O₂ - ANALYSIS IN AIR. W.K.R.Barnikol, W.Döhring, and K.Diefenthäler.Physiol. Inst. Univ. Mainz, 65 Mainz, West Germany.

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A Pt – electrode is described, that has a 95 % – response time of less than 20 ms, and thereby it is about 5 to 10 times faster as the O_2 – electrode in use up to now. Our electrode is characterized by three pronounced properties. Firstly it is covered with an extremely thin Teflonmembrane, which makes possible a short response time. The membrane is prepared according to a new method developed for this purpose. Secondly it has a fine adjustment which permits the cathode to be implaced upon the membrane with an advancement of $50\,\mu$ per turn in order to obtain maximum sensitivity. Thirdly there is a capability to easily change and center the cathode. The short response time of the electrode and its constancy can be put to use for the exact registration of very quick changes of O_2 concentrations. These changes occur in respiration physiology for example during hyperventilation.

ROLE OF DIFFERENT ZONES OF THE PRAYING MANTIS EYE. J.C. Barrós-Pita and H. Maldonado. Inst. Venezolano de Investigaciones Científicas, Caracas, Venezuela.

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The effect of blinding different zones of the praying mantis eye on its attack behaviour and on its deimatic reaction was analyzed. Adult females mantis Stagmatoptera biocellata were used. A special device, previously described and called the double-goniometer, was employed to localize those areas of the eye that were blinded. Results indicate: 1) that a special zone of the mantis eye is necessary and sufficient for a fine estimation of catching distance; 2) that the other zone is specially implicated in shape and/or movement discriminations; 3) that a lateral zone is responsible for the detection of an object entering in the visual field. These different zones proved to have some special morphological characteristics, i.e. radii of curvature, number of ommatidia per unit area and ommatitium area. In accordance with these data a model of the eye is presented and a functional explanation for the morphological characteristics of each zone is put forward.

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OXYGEN TRANSPORT IN EARLY EMBRYOS. <u>H. Bartels</u>, <u>F. Baumann and D. Dhindsa.</u> Dept. of Physiology, Med. Hochschule Hannover, Germany, Oregon Regional Primate Research Center, Beaverton, Ore. USA, Heart Res. Lab., Univ. of Oregon Med. School, Portland Ore., USA.

Before circulation is functioning oxygen supply to embryos can only be achieved by diffusion. Size of embryos should therefore be diffusion limited. The correlation between size of chicken or mouse embryos (stage 6-14) and oxygen consumption of different oxygen pressures was investigated with a platinum 0, electrode in 50 to loo µl-chambers. V_O, could be measured continuously via P_O, decrease. A diminishing rate of V_O, at a certain P_O (P_Ocrit) showed that the embryo is no longer supplied sufficiently with O_O by diffusion. For embryos without effective circulation P_Ocrit was 250 - 300 Torr, suggesting that chicken embryos at this stages at sea level are not sufficiently supplied with oxygen, and presumably gain part of the necessary energy by anaerobic glycolysis. The critical radius, calculated with a modified Warburg formula, using as diffusion constant K_O: 3,5 x 10 cm/min·atm., and measured QO, as well as P_O, shows good agreement with the morphological dimensions of the embryos investigated.

112 EFFECT OF COLD AND NORADREWALINE ON CARDIOVASCULAR CHANGES IN COLD ACCLIMATED RATS.

R. Bartůňková, L. Janský. Dept. of Comparative Physiology, Charles University, Prague, ČSSR.

In adult unanesthetized cold acclimated rats cardiac output and organ blood flow were measured during nonshivering thermogenesis induced by cold $(+6^{\circ}C)$ or by application of noradrenaline (NA), injected intramuscularly in a dose 0.4 mgNA/kg body weight at warm $(+26^{\circ}C)$ and cold $(+6^{\circ}C)$ environments. Exposure to cold increases cardiac output by 58% above to resting level, while application of NA at $+26^{\circ}C$, or $+6^{\circ}C$ enhances cardiac output by 99% or 90%, respectively. During exposure to cold or after applications of NA fractional distribution of cardiac output does not differ substantially from control animals. Due to enhancement of cardiac output absolute values of organ blood flow are generally enhanced in comparison with control animals. Differences were observed in blood flow in white and brown adipose tissues after application of NA or cold. Vasomotor changes caused by endogenous NA do not differ in principle from that induced by exogenous NA. Acclimation to cold leads to the activation of β -adrenergic receptors in the cardiovascular system.

A SYSTEM ANALYSIS OF THE EVOKED POTENTIALS IN THE ACOUSTICAL CORTEX. Erol Başar. Biol. Inst., Biophysics Unit, Hacettepe Univ., Ankara, Turkey

In order to obtain the frequency characteristics of signal transport in the auditory cortex of the cat, evoked potentials in the time domain are measured by applying suditory stimulations in the form of tone bursts of 700 Hz (acoustical step functions) and using chronically implanted electrodes in the middle ectosylvian gyrus. The evoked responses obtained in this way are characterized in the time domain by two positive peaks (Pland Pland Pland

114 ACTION OF OUABAIN ON SPLANCHNIC VASCULAR BED IN NORMAL DOGS. F.A. Bashour, A.M. Geumei. Cardiopulmonary Institute, Methodist Hospital, University of Texas at Dallas, Texas, USA.

Effect of Ouabain on Splanchnic Circulation was studied in intact dog (n=22) and in isolated liver preparation in normal (n=6) and in Phenoxybenzamine-pretreated (PNB) dogs (n=6). Hepatic blood flow (EHBF) was estimated using extraction-clearance technique of Bradley. Splanchnic blood flow (SBV) was calculated from mean circulation time and EHBF, reported as percent of total blood volume (SBV/TBV%). Systemic blood flow (CO), EHBF, mean systemic arterial (FA), hepatic vein (HV), and wedge (HW) pressures and resistances (systemic, total splanchnic, post sinusoidal) were determined at 10 min. intervals for 30 min. prior and 60 min. after 50 % I.V. Ouabain. Hepatic arterial (HA) and portal venous (PV) inflows were measured electromagnetically before and after Ouabain using constant perfusion pressure (120 mm and 10 mm Hg respectively.)

Ouabain increased FA (6%), HV (6%), HW (24%), and decreased EHBF (3-18%), CO (5-28%). It increased systemic (4-43%), total splanchnic (11-36%) and post sinusoidal (17-48%) resistances. SBV/TBV increased 4-13%. Ouabain did not affect HA but consistently decreased PV inflows (40-70%) and PNB failed to block it.

Ouabain constricted intrahepatic vessels, pooling blood in extrahepatic portal venous system with a resultant decrease in venous return.

SPLANCHNIC CIRCULATION DURING ACUTE RESPIRATORY ACIDOSIS. F.A. Bashour, A.E. Price, H.L. Gaspar, A.M.Geumei. Cardiopulmonary Institute, Methodist Hospital, University of Texas

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Effect of CO₂ breathing on Splanchnic Circulation was investigated in normal (n=11), splenectomized (n=8) and in normal dogs (n=12) pre-treated with Phenoxybenzamine (lmg/kg). Hepatic blood flow (EHBF) was estimated using extraction-clearance technique. Simultaneous measurements of EHBF, CO, mean systemic arterial (FA), hepatic vein (HV), and wedge (HW) pressures were made at 10 min. intervals before and for 30 min. after 8-10% CO₂ breathing. Splanchnic blood volume (SBV) was calculated from mean circulation time and EHBF, reported as percent of total blood volume (SBV/TBV%).

Hypercapnea increased HW (11-18%) and decreased FA (2-10%). EHBF and CO increased 46-87% and 4-17% respectively, while reducing total systemic (10%) and splanchnic resistances (30%). SBV/TBV decreased from 29.0% (control) to 17.4%. PNB abolished

Pesults indicate that hypercapnea constricted splanchnic venous and dilated splanchnic arteriolar systems. The behavior of splanchnic venous bed is mediated

PRESSOR RESPONSES TO VASOACTIVE AGENTS IN REMAL INFARCTION HYPERTENSION. Nidia Basso and I.J. de la Riva. Centro de Investigaciones Cardiológicas. Universidad de Euenos

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Cardiovascular reactivity in hypertension due to renal infarction was studied in 28 male Wistar rats (230 g). The animals had chronic cannulae in the abdominal aorta and jugular vein. Pressor responses to tyramine(0.1 mg), angiotensin(0.1, 0.4 and 1.6 ug), noradrenaline(0.25, 1 and 4 ug)and remin(0.05 GU) were obtained in the unanesthetized, untreated animals that were used as their own controls. Renal infarctions were produced in 22 of these rats by the ligature of a renal artery branch at both kidneys. Six untreated animals were followed as controls. Pressor responses were determined in all the animals twice a week during the three following weeks. 13 rats developed hypertension during the 2nd week after infarction. Pressor responses to all vasoactive agents tested were increased since the first day after renal infarction when animals were still normotensive. Increments were statistically significant for tyramine(45% P<0.001), nor-adrenaline(74% P<0.05, 68% P<0.025, 39% P<0.05) and remin(68% P<0.025). Renal infarcted rats that did not develop hypertension (9 animals) only increased their response to renin(45% P<0.01). Control rats did not change their pressor responsiveness. Renal infarction leading to hypertension seems to modify the sensitivity of vascular walls to vasoactive pressor agents, responses to noradrenaline and tyramine being the most remarkably augmented. This mechanism might be involved in the onset of hypertension since vascular hyperreactivity precedes the appearance of high blood pressure.

INTEGRATIVE FUNCTION OF LOTOR ANALYSOR. A.S. Batuev. Lab. of Motor Analysor, Inst. of Physiology, Leningrad State University, Leningrad, USSR.

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The cortical area of the motor analysor in cats is a collector of afferent impulses from various sensory systems. Under chloralose in the posterior sigmoid gyrus there was found out a great number of polysensory neurones to which converges both somatic, visceral and visual, auditory impulsation. Multimodal stimulations unlike monomodal ones reveal the change in the neural response pattern with the facilitation or occlusion phenomena. The probability of the efferent discharge appearance depends on the correlation of the parameters of the cortical surface and deep layers local /dendritic/ potentials. With rhythmical stimulation accompanied by the total cortical responses habituation, impulse activity of the deep layers neurones and descending pyramidal influences, the upper layers spontaneously. usly active neurones adopt the stimulation rhythm forming discharges preceding the stimulation. The cortical neurones of the motor analysor are supposed to be involved in the integrative brain system which is capable of accumulating the traces and regulating the organism reactions to a stimulus novelty.

THE EFFECT OF VARIOUS PARAMETERS ON THE ADHESIVENESS OF NEUTROPHILIC LEUCOCYTES TO GLASS SLIDES. W.Baudisch. Inst.of Physiology, Univ.of Rostock, GDR

Full blood from men is tested for adhesiveness of leucocytes (1). Neutrophilic granulocytes only are sticky. Their number depends on coagulation, time of incubation, temperature, and on the number of cells present in the blood. Metabolic inhibitors such as 2,4-dinitrophenol, iodoacetamide, or iodoacetic acid reduce the adhesiveness at an average of 83%, 57%, resp.12%. The results point to an active participation of metabolism of the cell in producing stickiness. Admixtures of 1 or 2x10-3M ATP to blood decrease the adhesiveness to 49% or 4% respectively. ADP and AMP fail to show significant results. The theories of P.C.T. Jones (2) and B. Norberg (3) are transferable to the granulocytic cell of the blood and are explaining their behavior by assuming an ATPase-like contractile protein in the membrane of the cells. 1) Baudisch, W., A.Beckmann, I.Blank, H.L.Jenssen, Acta biol.med.Germ. 23, (1969) p.265. 2) Jones, P.C.T., Nature 212, (1966) p.365. 3) Norberg, B., Exp.Cell Res. 59, (1970) p.11.

119 SPECIFIC BINDING OF ³H-ANGIOTENSIN II IN RABBIT ADRTA. <u>M. Baudouin, P. Meyer</u> and <u>M. WORCEL</u>. Hypertension Laboratory, Hopital Broussais, Paris 14, FRANCE.

With the use of highly labelled ^{3}H -angiotensin II a specific binder of angiotensin was demonstrated in the rabbit aorta. The binding fulfilled the characteristics of reversibility, great affinity, limited capacity and high specificity. The concentration of sites per mg of aorta is 8.4 ± 4.8 . 10^{-15}M . The kinetic constants of the specific binding were identical to those of the biological contractile response. The inhibitory ability of angiotensin derivatives on radioactivity incorporation was proportional to their respective biological activities. These observations suggest that the specific binding sites correspond to those involved in the biological response.

CONSTRUCTION OF HUMAN ARTERIAL PRESSURE AND FLOW PULSES BY MEANS OF SIM11. IFIED NON-UNIFORM TUBE MODELS WITH AND WITHOUT DAMFING. R.D.Bauer, Th.

Fasch, E.Wetterer. II. Physiol. Inst., Univ. Erlangen, Germany.

The genesis of the typical contours of central and peripheral arterial pulses can be demonstrated by means of simple non-uniform tube models (1, 2). These models consist of two or three uniform tubes arranged in series in such a way that the characteristic impedance increases by steps towards the end of the system. Wave reflexions occur at all sites of local change of impedance. The contour of the primary pulse wave is identical with that of the flow pulse generated in the ascending aorta by the left ventricle. The resulting contours of pressure and flow pulses are obtained by the superposition of primary and reflected waves. The model used in these calculations possesses four reflexion sites: one at the system's entrance, one at its end, and two within the system. One of these, placed near the entrance, is essential for the formation of the systolic part of the central pressure pulse. The calculations are carried out by a digital computer assuming undamped waves as well as frequency-dependent damping. The similarity of computed and natural arterial pulses is shown.

(1) Bauer, R.D., Th.Pasch, E.Wetterer, Verh.Dtsch.Ges.Kreisl.-Forsch. 36, 330, 1970. (2) kenner, Th., E.Wetterer, Pflügers Arch.Physiol. 275, 594

THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN EXPERIMENTAL LEFT HEART FAILURE IN THE DOG. J.S. Baumber and J.O. Davis, Dept. of Physiology, Univ. of Calgary, Alberta, Canada, and Missouri, Columbia, Missouri, U.S.A.

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The involvement of the renin-angiotensin-aldosterone system in isolated left heart failure and pulmonary edema (PE) has been studied. An 8 mm diameter teflon graft was sutured between the aorta and left atrium in 16 dogs and a loose ligature placed around the debetween the act to all the stress of the str was unchanged. Constriction of the aorta by tightening the ligature in 5 animals resulted in a transient rise in PRA which returned to normal in 4 days (5.5 ng/ml). The subsequent development of spontaneous PE in these dogs resulted in an average PRA of 47.8 ng/ml and an average LVEDP of 38 mm Hg. The administration of deoxycorticosterone acetate (DOCA) (15 mgm/day) to 4 dogs with LVEDP's over 35 mm Hg resulted in continuous sodium retention and the precipitation of PE. DOCA administration to 3 dogs with LVEDP's below 35 mm Hg resulted in only a transient retention of sodium and no clinical evidence of PE. of disappearance of H3-d-aldosterone from plasma was the same in 5 normal dogs (t1=23 min); of disappearance of n-u-algosterone from plasma was the same in 3 normal dogs ($\frac{1}{2}$ =20 min); and in 2 dogs with an average LVEDP of 38 mm Hg but with no evidence of PE ($\frac{1}{2}$ =20 min); and in 2 dogs with fulminating pulmonary edema ($\frac{1}{2}$ =22 min). In these latter 2 dogs the PRA was 80 dogs with full LVEDPL ($\frac{1}{2}$ =20 min). ng/ml and 31 ng/ml with LVEDP's of 57 and 45 mm Hg resp. These results indicate that PE is associated with the activation of the renin-angiotensin-aldosterone system but there is no indication that the metabolism of aldosterone is compromised.

PACEMAKER PROPERTIES OF COMPLETELY ISOLATED NEURONS IN <u>APLYSIA CALIFORNICA</u>. R. von Baumgarten and C. F. Chen. Mental Health Res. Inst., Univ. of Mich., Ann Arbor, Mich. 48104

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Completely isolated pacemaker neurons of Aplysia were obtained by immersing whole garglia in a solution of 0.25% trypsin in sea water at 35°C for three hours. They were then subjected to careful mechanical separation with microdissecting pins. Neurons with axons of up to several mm could be completely isolated from the surrounding tissue. The membrane potentials, spike amplitudes and firing patterns of the isolated neurons were similar to those of neurons in intact ganglia. Synaptic potentials were absent; consequently, the firing patterns were more regular than in the intact ganglia preparation. These methods provide an interesting opportunity for studying the endogenous pacemaker properties of neurons without interference from any synaptic input and without chemical or electrical influence from the surrounding tissue. Regular pacemaker activity was maintained in isolated cells over a period of more than 24 hrs. By lowering the Ca⁺⁺ concentration in the surroundingsea water by more than 80%, it was possible to convert isolated pacemakers from their original beating pattern into a bursting pattern. A similar conversion from beating to bursting was observed after the K⁺ concentration in the bath solution was increased. When the concentration of K⁺ was 15-20mM, bursting occured only temporarily. At a higher concentration (30-40mM), bursting was maintained permanently. These effects were accompanied by small transitory depolarization of the membrane. All these changes could be completely reversed by washing the neurons with sea water. It is suggested that similar shifts of Ca⁺⁺ or K⁺ are one possible mechanism governing the natural occurrence of the bursting pattern.

SYMPATHETIC AND VAGAL REFLEX RESPONSES DURING SLEEP AND WAKEFULNESS IN UNRESTRAINED CATS. W.Baust, J.Böhmke, and U.Blossfeld. Dept. of Neurology, University of Düsseldorf, Düsseldorf, W.-Germany.

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The purpose of this study was to investigate the excitability of central sympathetic and vagal neurons during sleep and wakefulness. Reflex responses in the vagal and sympathetic nerve were elicited by single stimuli applied to the mesencephalic reticular formation in cats with chronically implanted electrodes. The amplitudes of the sympathetic evoked response were diminished during synchronized sleep with respect to wakefulness; they showed a further, marked reduction during REM sleep. The vagal evoked responses had the largest amplitudes during synchronized sleep while the amplitudes of the potentials observed in wakefulness and REM sleep were almost identical. It can be concluded from these findings that synchronized sleep is the most vagotonic phase of sleep. The lowest sympathetic tone, however, is seen during REM sleep. Thus, vagal and sympathetic excitability does not take a strong, antagonistic course in relation to sleep and wakefulness.

124 FACTORS AFFECTING THE BRAIN FREE FATTY ACIDS (FFA). N.G. Bazán, Jr. Instituto de Investigaciones Bioquímicas, Universidad Nacional del Sur, Bahía Blanca, Argentina.

Brain FFA constitute a small and highly labile pool. Brief periods of ischemia produced a large increment in free unsaturated acids. This phenomena seems to be unique for the mature central nervous system since new-born rat brain, adult liver and spleen show a much slower rate of production. Squirrel monkey grey matter produced FFA at a strikingly rapid rate unlike white mater. Pentylenetetrazol-convulsant rats showed a highly significant increment in the brain FFA content, similar to the effect of a single electroconvulsive shock (ECS). Other convulsant drugs did not altered the free metabolite. 20:4, 18:0, 18:1 and 16:0 were freed at faster rates. Neither triacylglycerol breakdown nor a change in plasma FFA appear to be responsible for the major part of the increment. The ECS effect was abolished by ether anesthesia.

DISPLACEMENT OF ELEMENTS WITHIN MAMMALIAN MUSCLE SPINDLES. W.S. Beacham, Y. Fukami,

C.C. Hunt and D. Ottoson. Dept. of Physiology and Biophysics, Washington Univ., St.

Louis, Mo., U.S.A.

Using a Zeiss Nomarski interference contrast microscope and high speed photography, the displacement of sensory terminals and intrafusal fibers of isolated mammalian muscle spindles has been studied in vitro. Annulospiral (primary) endings can be clearly visualized. Stretch, of ramp and hold configuration, causes displacement of these terminals which, at this level of resolution, shows no consistent phasic component that would account for their known dynamic response. The technique is also being used to measure the movement of intrafusal muscle fibers when directly or indirectly stimulated. Preliminary results indicate differences in the contractile responses of large (bag type) or small (chain type) intrafusal fibers.

126 SODIUM FLUXES IN RAT RED BLOOD CELLS, <u>L.A. Beaugé and Olga Ortiz</u>, División de Biofísica, Inst. de Invest. Med. M. y M. Ferreyra, Córdoba, Argentina

The sodium content in rat red cells as determined by flamephotometry was found to be 4.40 $^\pm$ 0.11 m.mole/1.cells with a water content of 64.03 $^\pm$ 0.67 per cent, which represents 6.87 m.mole/1.water.Incubation for 60 min.in K (Rb)-free sodium Ringer resulted in a gain of 4.82 m.mole/1.cells sodium, whereas after incubation in K(Rb)-free choline Ringer the cells had lost 2.91 m.mole of sodium.Thus, short periods of time produced noticeable changes in the cells sodium when K(Rb) was absent.In sodium Ringer, 5 mM-Rb was able to maintain a steady intracellular sodium of about 5.40 m.mole/1.cells.The rate constant for 22 Na efflux was determined in different K(Rb)-free media in the presence or absence of 10-4 M ouabain.In sodium media the value was 1.044 $^\pm$ 0.072 hr⁻¹ and was reduced 77 % by ouabain.The sodium-free effect on this rate constant was variable depending on the substance used as a replacement; thus, in choline there was a 12% reduction, whereas it reached 62% reduction in magnesium.In all cases a variable ouabain-sensitive fraction was present.

NEUROPHYSIOLOGICAL MECHANISMS OF RELIABILITY OF MAINTAINING MENTAL ACTIVITY IN MAN. N.P. Bechtereva, V.M. Smirnov, V.A. Tchernysheva. Inst.for Exptl. Med. Acad. Med. Sci. USSR, Leningrad, USSR.

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Use of implanted electrodes in clinic provided premises for studying the neurophysiological mechanisms of various kinds of activity
including mental. By means of elaborated oomplex method, over I200
small areas within the deep brain structures were studied. This gave
ground to suggest that the mental activity is maintained by a cortical-subcortical structural-functional system with links of different degrees of rigidity, and to consider the mechanisms of reliability of maintaining this activity. Abundant reserves of the system of control of the mental functions are represented in spatial mosaics of varying (flexible) links of the system that are involved when changes in the evironment occur. The reliability of the system increases on account of its polybiochemical character. Sustaining of conditions for maintained mental activity is realized through an apparatus of "regimen regulation" consisting of structures of activating and inhibitory types which alter the regimens of the mental activity on principle of mutually complementing and shunting influences. influences.

SYMPATHETIC NERVOUS INFLUENCE ON ALVEOLAR SURFACTANTS AND LUNG COMPLIANCE. David L.

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Beckman, John W. Bean and Donald R. Baslock. The Univ. of Michigan, Highway Safety
Research Institute, and Dept. of Physiology, Ann Arbor, Michigan 48105 USA.

It has been shown that lethal mechanical head injury (captive bolt) decreases lung compliance in Squirrel monkeys by 50% in the absence of any attendant gross lung pathology (Fed Proc 29:594, 1970); that this compliance decrease, and gross lung changes in rats, can be prevented by pretreatment with sympatholytic agents (J Appl Physiol 28:807, 1969; 20:631, 1970), but not with isoproterenol or atropine eliminating smooth muscle effects, and that these changes are absent from saline P-V curves (Physiologist 13:145, 1970). The present experiments were carried out in a further investigation of a sympathetic nervous influence on alveolar surfactants. Electrical stimulation (12 V.; f. 60/sec; 3 msec duration) of the stellate ganglion in 8 monkeys anaesthetized with ketamine (Parke-Davis) or head injury in 10 monkeys did not alter lung wt/body wt ratios, but caused a 40-60% in vivo compliance decrease, a high minimum surface tension (>22 dynes/cm), and smaller hystogosis loop areas in the calling lung wish accompanion (>22 dynes/cm). cm), and smaller hysteresis loop areas in the saline lung wash, compared to sham operated controls or the contralateral lung. These changes were blocked by pretreatment with Dibenzyline. Central hemodynamic factors were largely ruled out by tests in which pressures were held constant in the catheterized aorta and central vena cava during and after this head injury. The data support the earlier interpretation (Fed Proc 29:594, 1970) that alveolar surfactants and total lung compliance are in large part under sympathetic control. (Supported by NIH-RG-GM-16912 and HE-01646)

EXERCISE DEAD SPACE - A ROLE FOR LAMINAR FLOW? J. M. Beeckmans and Roy J. Shephard. Fac. Eng. Sci., Univ. West. Ont., and Dept. Phys. Hyg., Univ. Toronto, Ont.

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Models based on the assumption of a square wave-front of inspired gas lead to substantial over-estimation of the anatomical dead space during both rest and exercise; discrepancies are reduced but not abolished by a model that uses an intermediate flow pattern and makes appropriate allowance for changes in the dimensions of the airway with respiration. It is suggested that the mixing of alveolar and bronchiolar gas is speeded by laminar flow in the small air passages. A fair description of experimental results is given by the equation

 $V_D = V_f + (V_e - 200) e^{-Kt}$

where VD is the effective volume of the anatomical dead space, Vf is the volume of the conducting airways to the level of the fifteenth order bronchioles, Ve is the volume from the sixteenth order bronchioles to the third order alveolar ducts, 200 is an arbitrary correction for laminar gas flow, K is a diffusion constant (1.0 for nitrogen, 0.8 for carbon dioxide), and t is the half-length of the respiratory cycle, measured in seconds.

NUMERICAL RECONSTRUCTION OF THE MYOCARDIAL ACTION POTENTIAL. G. W. Beeler, Jr. Dept. of Physiology and Biophysics, Mayo Graduate Sch. of Medicine, Rochester, Minn. USA.

Recent experimental data from several laboratories, including our own, have been combined in a numerical model of the myocardial action potential. This model involves: one steady and two time-varying components of outward potassium current; a dynamic inward sodium current; and a dynamic inward calcium current. The potassium current dynamics were adapted from experiments performed in D. Noble's laboratory (e.g. D. Noble & R. Tsien, J. Physiol. 200:233, 1969.) Where possible, sodium and calcium dynamic parameters were determined from our data (G. Beeler & H. Reuter, J. Physiol. 207:165 & 191, 1970.) The activation time constants for the dynamic calcium current were estimated from our experimental data, and from the rate of repolarization of the simulated action potential. An unspecified mechanism was assumed to bind calcium so as to reduce the internal concentration to a level of 10-7M with a fixed time constant. The resulting reconstruction matches well a standard action potential, and demonstrates normal interval-action potential duration relations. The plateau phase in the simulation was shown to result from the competition between a slowly developing outward current, and an inward calcium current undergoing inactivation. The model was also used to study mechanisms by which premature regenerative repolarization might be induced experimentally. Such studies aided in the designof experiments to verify the estimates of calcium current time constants. (Partially supported by USPHS Grants FR00007, and HE12824.)

A PLASMA PROTEIN PRODUCING ANOREXIA IN THE RAT. L. W. Belbeck and J. A. F. Stevenson. Dept. of Physiology, Univ. Western Ontario, London 72, Ontario Canada.

Previously, an extract of urine from fasting animals was observed to have anorexigenic activity. A homogeneous preparation of this compound has now been obtained and a glycopeptide structure hypothesized following characterization by staining reactions, absorption spectra, and amino acid and carbohydrate analyses. To demonstrate the anorexigen in serum, plasma proteins were precipitated with 0.6N perchloric acid but the anorexigen was precipitated from the supernatant only by the addition of ethanol. The precipitate was redissolved in 0.lN sodium hydroxide and either purified on a Sephadex G-75 column or the amount present estimated by determining the hexose by the anthrone method. The compound had a sedimentation coefficient of 1.5 and formed a precipitation line in the alpha-2 globulin region using immunoelectrophoresis. In vivo, 2mg/100g body weight of the anorexigen given intraperitoneally produced a suppression of food intake lasting 24 hours with a concomitant weight loss. The animals neither became refractory following repeated injections nor formed precipitating antibodies. In the conscious rat, intravenous administration produced a dose-related reduction in food intake and blood glucose concentration (GL) with an elevation of serum free fatty acids (FFA) one hour postinjection. Animals food deprived for 24 hours, injected, and then fed, ate a small amount: GL increased and FFA decreased but total food intake remained markedly reduced.

132 EFFECT OF POSTJUNCTIONAL POLARIZATION ON THE LEECH GANGLION CELLS INTER-ACTION. Bogdan B.Beleslin. Dept.of Pathological Physiology, Med.Fac., Beograd, Yugoslavia.

The effect of the postjunctional polarization, on R e t z i u s nerve cells interaction of leech, was investigated in the normal, rubidium (KCl replaced by RbCl) and tris (NaCl replaced by tris-Cl) leech R i n g e r 's solution. Four microelectrodes, filled with 3 M K-Acet, were inserted into a pair of cells. Two of them, were used for sending simultaneously, rectangular pulses (800 msec.duration) on the pre, and constant polarizing current (40 sec.duration) on the postjunctional side. It was found, that in the normal and rubidium leech saline, constant polarization of the postjunctional side caused a decrease of membrane resistance of directly polarized and nearby cell. The coupling coefficient fell too. The propagation of impulses from cell to cell was blocked by the postjunctional hyperpolarization. On the other hand, in the tris R i n g e r 's solution an increase of membrane resistances were obtained and constant polarization of the postjunctional side was less effective in dropping coupling coefficient.

IONIC REQUIREMENTS FOR THE PERISTALTIC REFLEX OF THE GUINEA-PIG ISOLATED ILEUM. D.B. Beleslin. Dept. of Pharmacology, Medical Faculty, Beograd 11105, Yugoslavia.

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In these experiments the importance of sodium, potassium, calcium and magnesium ions for the peristaltic reflex was studied. For recording the peristaltic reflex Trendelenburg's method was used. The peristaltic reflex was elicited by increasing the intraluminal pressure by 3-4 cm H₂O for about 90 sec at constant time intervals. The sodium-free or deficient solutions were prepared with Tris chloride. In calcium, potassium and magnesium were completely or partly omitted, but with other salts present in the Tyveloped in 10 min., while in a potassium-free solutions peristaltic block deto produce a block. The peristaltic reflex was not inhibited, however, when the evidence is presented that sodium, potassium and calcium ions are essential for the peristaltic reflex.

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CORRELATED FIRING AMONG CLIMBING FIBERS AND ITS SPATIAL DISTRIBUTION ON THE CEREBELLAR SURFACE. C. Bell and T. Kawasaki. Good Samaritan Hospital, Portland, Oregon, U.S.A. The spatial and temporal pattern of incoming climbing fiber activity was studied in the vermis of guinea pigs, lightly anesthetized with pentobarbital. Spontaneously occurring climbing fiber responses (CFR's) were recorded from two or three Purkinje cells simultaneously. Separate micropipettes were used and the distance between them as well as their orientation with respect to the folium was varied. A total of 96 pairs and 6 triplets were recorded. Correlated pairs of CFR's were found at much greater distances in the transverse direction of the folium (perpendicular to the parallel fibers) than in the longitudinal. We suggest that the correlation between climbing fiber discharges arises from shared input to inferior olivary cells, and that recurrent collaterals of other olivary cells are the main source of the shared input. This is supported by a statistical argument, by the finding of similar correlations in the inferior olive and by the following additional result. Synaptically evoked responses of climbing fibers could be elicited by electrical stimulation of nearby points on the cerebellar surface and such points showed a spatial distribution similar to that of the spontaneous correlations. We conclude that the intrinsic synaptic organization of the inferior olivary nucleus results in correlated discharges among those climbing fibers which project onto sagittal strips of cerebellar cortex. (Supported by NIH grants NB-06728 and NB-02289.)

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PHYSIOLOGICAL STRUCTURE OF THE VISCERAL EFFERENTIAL AREA OF THE CAT LIMBIC CORTEX AND THE CEREBELLUM. N.Beller, V.Chernigovsky, M.Talan. Pavlov Inst. of Physiology, Acad. of Sciences of USSR, Leningrad, USSR. Three limited zones are detected within the 24-th a. 32-th cytoarchicectonic area of the rostral parts of the limbic cortex by means of electronic area of the rostral parts of the limbic cortex by means of electronic area of the rostral parts of the limbic cortex by means of electronic area of the rostral parts of the limbic cortex by means of electronic area of the rostral parts of the limbic cortex by means of electronic area of the rostral parts of the limbic cortex by means of electronic area of the rostral parts of the limbic cortex by means of electronic area.

Three limited zones are detected within the 24-th a. 32-th cytoarchitectonic area of the rostral parts of the limbic cortex by means of electrical stimulation. Stimulation of each of these zones exerts a specific action on blood pressure and the motor activity of the intestine and the urinary bladder. Stimulation of one of the zones exerted ingibitive effects, that of the second - excitation ones and the third zone got mixed effects. Within the zones still more localized points were found which provoked stronger pronounced reactions, these being codified as focuses of Maximum Reaction (FMR). Similar effects were observed when certain zones of cortex cerebellum were electrically excited. The study of the effects caused by the stimulation of nuclei cerebellum (n.fastigius, n.interpositus and n.dentatus) made it possible to find similar zones in cerebellum subcortical structures. The effects caused by cortex stimulation are supposed to by realised through specifical zones of the nuclei of the cerebellum. The latter are involved in the mechanism of the transmitting the effects from the cortex of the cerebellum to the effectory visceral systems.

136 EFFERENT FIBERS IN THE AORTIC NERVE. C. Belmonte, J. Simón and R. Gallego Dept. of Physiology. Med. Sch., University of Madrid, Madrid-3 (Spain).

Electrical activity showing a cardiac rythm was recorded in the central cut end of the left aortic nerve (30 cats). It appeared 60-80 msc.after the R wave of the ECGintravenous norepinefrine and intraaortic saline injection increased the electrical activity which was deseased with homolateral carotid occlusion. Electrical stimulation of the preganglionic trunk of the stellate ganglion gave a potential complex recorded in the thoracic part of the left aortic nerve; it was abolished by intravenous ganglion-blocking agents and reappeared with postganglionic stimulation. Conduction velocities of activated fibers ranged 1.2-3 m/sec. Preganglionic stimulation of the cervical sympathetic trunk gave a low-threshold response conducted at 15-42 m/sec. This response was not modified by ganglion-blocking agents or by cutting of the sympathetic, cranial to the stimulating electrodes. A modification in the baroreceptor discharges was observed during stellate ganglion stimulation before arterial pressure changed, and also when a small strand of the aortic nerve was recorded during the electrical stimulation of the remainder fibers in the peripheral cut end of the nerve. These results suggest the existence of efferent fibers in the aortic nerve: in part C-sympathetic originated in the stellate ganglion, which when stimulated could modify the baroreceptor response of the aortic sinus

THE PHYSIOLOGICAL EFFECTS OF SUCROSE ADMINISTRATION DURING PROLONGED EXERCISE OF MODERATE INTENSITY. A.J.S. Benade and G.G. Rogers. Human Sciences Lab., Chamber of Mines of South Africa, Johannesburg, South Africa.

Four young fit men worked for six hours on a bicycle ergometer at 45% of their maximal oxygen uptake. When they received only water, R.Q. decreased continuously during work. Plasma free fatty acids increased three-fold. Aceto acetate and 3-OH butyrate in blood showed a four-fold increase during six hours work. A continuous increase in oxygen uptake and heart rate accompanied the increased fat metabolism. When the men received water and 100 gm sucrose at the end of the third hour of work, R.Q. rose within fifteen minutes after ingestion. R.Q. remained significantly higher compared to when the men received only water. The sucrose was mixed with 100 µc uniformly labelled C14 sucrose and the C1402 in expired air followed R.Q. closely. A further increase in circulating F.F.A. after the third hour was delayed. Aceto Acetate concentration remained high, in contrast to 3-OH butyrate which declined to low levels as compared to the no-sucrose experiment. The relative change from mainly fat to mainly carbohydrate metabolism was evidenced by significantly lower oxygen uptakes and heart rates during the last two hours of work.

MICROPUNCTURE STUDY ON THE MECHANISM OF THE DIURESIS AND NATRIURESIS FOLLOWING RENAL DENERVATION IN THE RAT. P.Bencsath, J-P.Bonvalet, C.de Rouffignac, with the technical assistance of P.Philippe. Dept. of Biol., CEN-Saclay, 91, France.

The distribution of single glomerular filtration rate (SGFR) was studied in both kidneys of 2 nondiuretic and 4 isotonic saline loaded rats (14-C ferrocyanide technique, 500 nephrons dissected) after acute unilateral renal denervation. In other 5 nondiuretic animals late proximal and early distal tubules were punctured in the left kidney before and after denervation, urine from both kidneys being continuously collected. Denervation was followed by significant diuresis and natriuresis in any of the experiments with no difference in filtration rates between intact and denervated kidneys. Superficial and juxtamedullary SGFR's remained unchanged, excluding thus the possibility of a redistribution in glomerular filtration. (TF/P)In proximal as well as distal significantly decreased (2.60+0.71 S.D. to 1.72+0.28 and 6.68+2.44 to 3.93+1.42, respectively, P<.001, (TF/P)Na and (TF/P)K distal increased (0.31+0.07 to 0.41+0.07 and 0.40+0.04 to 0.48+0.09, respectively, P<.001-<.01) on denervation, while the increase in (TF/P)osm distal and the decrease in (TF/P)Urea were not significant. In 10 experiments, where cortico-papillary sodium and urea gradients were also determined, the greatest differences in water and electrolyte excretion between the two sides were associated by a decrease in gradients of the denervated kidney. These results yield direct evidence that denervation impairs transtubular sodium transport in the proximal tubule and possibly in the loop of Henle and suggest that haemodynamic changes are of secondary importance.

INDUCTION OF PROLACTIN RELEASE IN JUVENILE RATS BY PERPHENAZINE. M. Ben-David. Dept.of Applied Pharmacology, Sch.of Pharmacy, Hebrew Univ. Jerusalem, Israel.

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Mammary growth and secretion were induced in rats by perphenazine treatment (5mg/kg/day, for 5 days). This effect was found to be associated with pituitary (5mg/kg/day,10r) days,... effect was found to be associated with productin release (Ben-David, M., Endocrinology 83:1217,1968). In order to assertain whether juvenile rats can also discharge productin in response to assertant whether juvening the data also discharge profactin in response to perphenazine, a single injection of the drug (10mg/kg) or saline was given to rats aged 12 to 35 days. One h later all animals were killed by decapitation and pituitary and serum prolactin was measured by radioimmunoassay. Considerable amounts of prolactin were found to be present in the pituitaries of control animals(250-1300ng/pit.) but only a minute amount (0-6 ng/ml) was detected in the serum.Perphenazine caused immediate release of prolactin from the pituitary into the blood of all groups tested, becoming pronounced after the age of 20 days. A similar trend of reaction was found in both female and male animals, namely, serum prolactin highly increase (20-85 ng/ml) while pituitary prolactin concomitantly decreased (130-950 ng/pit.). These results suggest that rats normally produce prolactin before sexual puberty, but release only sub-threshold doses into the blood stream because of strong and tonic hypothalamic inhibition. Once this inhibition is reduced by perphenazine treatment or by natural maturation, the pituitary is free to release high prolactin amounts into circulation.

RECHERCHES DES FONCTIONS NERVEUSES CENTRALES PAR LA MÉTHODE EREG CHEZ LES CHIENS. A.Benetato, E.Daneliuc et R.Vrîncianu. Institut de Physiologie Normale et Pathologique "D.Danielopolu" de l'Académie des Sciences Médicales-Bucarest, Roumanie.

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L'électrorétinogramme spontané et les potentiels évoqués occipitaux enregistrés pendant les stimulations visuelles colorées (méthode EREG) peuvent servir, chez les animaux tout comme chez l'homme, à établir l'état d'excitabilité (E) et d'inhibition (I) nerveuse centrale. Chez les chiens normaux sont préférables les explorations en saison automnale, puisqu'elles procurent des réponses quasi-uniformes qui peuvent être employées à déterminer les valeurs normales de l'excitabilité et de l'inhibition nerveuseminer les valeurs normales de l'excitabilité et de l'inhibition nerveuse-centrale (chiffres témoins en ms). Par contre, on trouve de larges varia-tions individuelles, dûes à l'âge et surtout à la période oestrale, pendant le printemps. Chez les jeunes femelles, la période oestrale s'exprime par une nette vagotonie décélable életrophysiologiquement. Oscillographe cato-dique "Toenus", Stimulateur "Alvar", filtres colorés.

INFLUENCE OF AGE ON THE PHYSICOCHEMICAL STATE OF BRAIN PROTLINS. Gr. Benetato, M. Uluitu, Gh. Petec. Institute of Normal and Pathological Physiology, Bu-

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charest, ROMANIA. We showed earlier that proteins extracted by centrifugation(loo.coo G) from reflex stimulated rat brain cortex homogenate exhibit characteristic biophysical changes: decrease of buffering capacity (BC)=mMHCl/1 g protein/ ApH, low degree of undiffusible -COO groups dissociation evaluated by protein proton titration curve according to Linderstrom-Lang's theory and the eq.: pH=pK int + log. $\alpha/(1-\alpha)$ - 0.868 WZ. Thus stimulation results in a diminution of undiffusible-COO -groups polarization leading to their reduction in K affinity. This fact was also down strated by assays of in reduction in K-affinity. This fact was also demonstrated by assays of intra-and extracellular K in terms of the inulinic space as well as of CSF K (Rev. Roum, Physiol. 1970, 7, 95). The present work was performed in senile (Rev.Roum.Physiol.1970,7,95). The present work was performed in senile (1), adult(2) and newborn(3) rats to study pK.int. variations and BC of brain proteins. We found that age induces a deionization of -COO groups in senile brain proteins: higher pK(4.675) as compared to adult(4.52), low BC and shift of the izoelectric point towards alkalinity.

These protein physicochemical changes and brain K mobilities again or found previously (Hoppe-Sayler Tierfelder Hand.der

zation found previously(Hoppe-Sayler Tierfelder Hand.der Physiol.Path.Chem.Auflage, BV,10, 526 could be accounted for by an increase in anionic field strength by deionization of Protein-COO groups.

RECHERCHES BIORADIOTELEMETRIQUES SUR LA REACTIVITÉ CARDIO-VASCULAIRE AU COURS DU TRAVAIL, CHEZ LES MÉTALLURGISTES. Prof.Dr.Gr.Benetato (Ing.R. Vrîncianu, Dr.Val.Ionescu, Dr.Ana Adameche). Institut de Physiologie Normale et Pathologique "D.Danielopolu" de l'Académie des Sciences Médicales, Bucarest, ROUMANIE.

QUALITATIVE AND QUANTITATIVE ASPECTS OF BINOCULAR INTERACTION IN CORTICAL AREAS 17 AND 18. L. A. Benevento, O.D.Creutzfeldt and U. Kuhnt. Max-Planck-Institute for Psychiatry, 8 Munich 23, German Fed. Rep.

Intra- and extracellular recordings were made in areas 17 and 18 in order to determine to what extent the functional properties of cortical neurons influenced by the 2 eyes are identical both qualitatively and quantitatively. Paralyzed cats faced a tangent screen and their eyes fitted with corrective contact lenses. Prism compensators were fixed in front of each eye for correction of divergence. Foveas, discs and stimuli were projected onto the screen. For each eye the receptive field of a neuron was determined by hand. Quantitative measurements were accomplished with automated stimuli and responses computer-analyzed. In addition to the known ocular dominance differences it was found that the qualitative receptive field organization for each eye can be different (e.g., a cell may be excited through on-center fields in one eye and through on- and/or off-center ones in the other). Other examples show an astonishing similarity in the inputs to one cell from the 2 eyes. During binocular stimulation the 2 monocular responses may add or certain aspects of one monocular response may be suppressed. Also the ocular dominance of a neuron can change with the type of stimulus. The findings indicate that the functional properties of individual cortical cells are determined mainly by direct afferent inputs from each eye but excitatory and inhibitory intracortical connections between different cell groups have a modifying effect.

144 INOTROPIC EFFECT OF SYMPATHOMIMETIC AMINES AND CARDIAC ADENYL CYCLASE ACTIVITY.

B.G. Benfey. Dept. of Pharmacology and Therapeutics, McGill University, Montreal,
Canada.

The theory that the effect of sympathomimetic amines on cardiac contractility involves the activation of the enzyme, adenyl cyclase, which catalyzes the conversion of ATP to cyclic AMP, was tested in rabbit ventricle slices incubated with dopamine or 1-phenyl-ephrine after pre-incubation with $^{14}\mathrm{C}$ adenine. The inotropic effect of the amines was evaluated in strips of rabbit left atrial appendage. It was found that the inotropic efficacy of dopamine and phenylephrine was similar to that of noradrenaline, that their inotropic potency was less than that of noradrenaline, and that only noradrenaline (0.01-1 mM) increased the rate of formation of cyclic AMP. This result makes it doubtful whether the activation of adenyl cyclase is an essential step in the inotropic effect of sympathomimetic amines. Dopamine lacks the β -hydroxyl group of noradrenaline and phenylephrine lacks the p-hydroxyl group of adrenaline; it appears that the 3 hydroxyl groups of the common catecholamines are required for the activation of adenyl cyclase. (Supported by the Medical Research Council of Canada.)

IMPORTANCE OF INERTIAL LOSS RATHER THAN FAHRAEUS-LINDQVIST EFFECT IN CANINE LIMB PERFUSION. A. M. Benis, S. Usami, K.-M. Jan and S. Chien, Lab. of Hemorheology, Dept. of Physiology, Columbia University, New York City, U.S.A.

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Since the work of Whittaker and Winton (J. Physiol. 78:339-369, 1933) on the canine hindlimb, the discrepancy between blood viscosity measured in isolated tissue and in laboratory viscometers has been attributed to the Fâhraeus-Lindqvist effect. In the present study, isolated canine hindlimbs were perfused under conditions of steady flow with (a) suspensions of red cells in albumin-Ringer solution (Hct = 0 to 80%), and (b) cell-free plasma expanders of different viscosities. Inertial losses in the hindlimb were computed on the assumption that they vary with the square of the flow rate. The results indicate that inertial losses, rather than a Fâhraeus-Lindqvist effect, may explain the discrepancy observed by Whittaker and Winton, in support of our earlier study on the canine hindpaw (Circ. Res. 27:1047-1068, 1970).

Supported by a Contract from the U.S. Army and Grants from the National Institutes of Health and The Scaife Family Charitable Trusts of Pittsburgh, Pa.

EFFECTS OF EXOGENOUS LIVER LYSOSOME SUSPENSION IN NORMAL DOCS. S.Benkő, T.Barankay, I.Szabó, Zs.Sebők, K.Benkő and G.Horpácsy. Inst. of Experimental Surgery, Inst. of Biology and 2nd Medical Clinic, University Medical School, Szeged, Hungary.

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Numerous authors have found that in various forms of shock lysosomal enzymes are released and several of them suggest their pathogenetic role. In our experiments fresh lysosome fraction isolated from dog liver was given intravenously to normal narcotized dogs. Besides the circulatory parameters the behavior of lysosomal acid phosphatase as marker enzyme was studied in the plasma. Besides negligible changes in blood pressure a small, but significant increase of the hematocrit was observed. The introduction of lysosome suspension significantly raised the plasma level of the acid phosphatase and the raised level remained stationary during the 150 minutes of the examination. The rise of the acid phosphatase level of the plasma caused by the introduction of the lysosome suspension was not influenced by the kallikrein inhibitor /Trasylol/ but under its influence the enzyme level began to decrease after 30 minutes and the decrease was continuous during the 150 minutes of the examination, but did not reach the control level. According to our investigations exogenous lysosome suspension cause no shock symptoms in healthy dogs. Thus it remains an open question what the pathogenetical importance of lysosomal enzymes is in shock.

GEOMAGNETISM AND CIRCADIAN ORGANIZATION IN EARTHWORMS. Miriam F. Bennett and Jan Huguenin. Dept. of BIOLOGY. Sweet Briar Col., Sweet Briar, Va., 24595. USA.

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Earthworms, <u>Lumbricus</u> <u>terrestris</u>, L., maintained in darkness and under constant conditions of temperature and humidity, crawl faster and withdraw from bright light faster during evening test-periods than during midday periods. The difference between the rates ranges from 18 to 48 percent, and on an annual basis averages 25 percent. Earlier work has proved that an intact central nervous system is necessary for the mediation of the circadian differences. The natural magnetic flux of the earth is also necessary for that difference in rates of the light-withdrawal reaction, for the difference disappeared when worms were maintained under constant laboratory conditions which included a magnetic field of essentially zero or one which was twice the force of the earth's field. During a 3-month study in autumn, worms in the zero field withdrew from light at the same rates during the midday and evening tests, while their controls in the earth's normal field were 20 percent faster in the evening. During a 2-month study in the spring, worms which lived in the natural geomagnetic field were 36 percent faster in the evening. Those which were maintained in the field twice that of the earth withdrew from the light only 8 percent more rapidly during the evening tests. Geomagnetism does have an effect on the circadian organization of <u>Lumbricus</u>. The site and the nature of that effect are unknown.

148 EFFECTS OF OSMOTIC PRESSURE ON THE RELEASE OF TRANSMITTER AT THE NEUROMUSCULAR JUNCTION. Pierre R. BENOIT, Laboratoire de Physiologie Générale, Faculté des Sciences - 91 - ORSAY - FRANCE.

Spontaneous release of acetylcholine increases when the osmolarity of the saline bathing a neuromuscular jonction is increased, but no clear effects of hyperosmolarity on the transmitter release evoked by a nerve impulse have been reported. In the present experiments, frog neuromuscular junctions were bathed in a low Ca⁺⁺Ringer to obtain an initial low quantal content of the end plate potential (e.p.p.). Increase of the osmolarity by adding sucrose to the Ringer caused increase of both spontaneous and evoked release of transmitter. When the osmolarity was increased from 10 to 40%, an exponential relationship between releases and osmotic gradient was observed, the relative increase in evoked release being lower than the increase in spontaneous release. The relative augmentation of quantal content of the e.p.p. was equal to the square root of the increase of the miniature e.p.p. frequency. In different junctions bathed either by normal or hyperosmotic solutions, a good correlation between the miniature e.p.p. frequency and the quantal content of the evoked e.p.p. was also observed. These quantitative relationships between spontaneous and evoked release of transmitter support the hypothesis that quantal release by nerve impulse corresponds to an accelerated form of spontaneous release.

149 COMPENSATORY EYE MOVEMENTS PRODUCED BY ANGULAR OSCILLATION. A.J.Benson. Royal Air Force Institute of Aviation Medicine, Farnborough, Hants, U.K.

In man, sinusoidal angular oscillation about a longitudinal (z) body axis was used to stimulate the lateral semi-circular canals and evoke compensatory eye movements. The gain and phase relationships of stimulus to response were found to be in general accord with a linear, second order system, model of the semi-circular canals at frequencies below 0.5 Hz. In the frequency band 0.02 - 0.5 Hz the gain of the vestibulo-ocular reflex was about 0.7 with the eyes closed, but when the eyes are open this can be supplemented by the fixation or pursuit reflex so that visual acuity is not degraded when the head is turned. At frequencies above 0.5 Hz a rapid decrement in the pursuit reflex is compensated for by an increase in gain of the vestibulo-ocular reflex, which was found to have a gain of 1.0 without apparent phase error at 3.0 - 5.0 Hz. Studies of subjects' ability to read stationary visual test material, whilst exposed to angular oscillation at 0.5 - 10 Hz, showed that visual stabilization by canal mechanisms was not impaired until at least 6.0 - 8.0 Hz.

PHYSIOLOGICAL AND BIOCHEMICAL STUDIES ON PINEAL ANTIGONADOTROPIN (PAG). B. Benson, M.J. Matthews, and J.T. Norris. Dept. of Anatomy, Univ. of Texas Med. Branch, Galveston, U.S.A.

Although certain pineal indoles are considered to be antigonadotropic agents, there are reports that pineal polypeptides are active also. In the present study aqueous extracts of adult rat or bovine pineals were given by i.p. injection on the day of unilateral ovariectomy (UO) to young adult, Charles-River CD-1 mice. This treatment resulted in the blockage of compensatory ovarian hypertrophy (COH) after 9 days. A molecular weight separation of aqueous extracts of bovine acetone pineal powder was made by ultrafiltration methods and PAG was found in molecular weight (MW) fraction 500-1000. Melatonin, determined by fluorometric methods, was found only in the MW fraction < 500. This latter fraction demonstrated no antigonadotropic activity. PAG was partially purified by aqueous methanol and isobutanol extraction. With gel-filtration on Sephadex-G25 a single ninhydrine-positive peak was seen to contain the PAG. The partially purified material blocked the gonadotropin-stimulated increase in ovarian weight and 32p uptake in the UO or hypophysectomized animal. These studies suggest that a small polypeptide is produced by the pineal gland with potent antigonadotropic activity. By comparison on the basis of weight, the activity of PAG in partially purified form is estimated to be 70-100 times that of melatonin. These data reinforce earlier reports by others that a small polypeptide has antigonadotropic activity.

Transmission in the perfused hypogastric ganglion. G.A. Bentley, Dept. of Physiology, Monash University, Victoria, Australia.

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A preparation has been developed whereby the hypogastric ganglion of the rat or guinea-pig may be perfused with physiological saline via its vasculature. By ligating the base of the vas deferens, the effects of injected drugs can be confined to the ganglion, while contractions may be recorded from the unperfused part of the vas. This provides a means for the study of transmission in this ganglion. Differences have been found between the cat superior cervical ganglion and the guinea-pig hypogastric ganglion. The latter is very insensitive to non-nicotinic stimulants, even when given etc., that are known to sensitise the cat ganglion to these drugs. However, after anti-cholinesterase treatment, or when tachyphylaxis to DMPP has drugs also cause a temporary reversal of this nicotinic desensitisation, as does preganglionic stimulation, which is still fully effective during the drug-induced tachyphylaxis. In the rat, the hypogastric ganglion was found to be more sensitive to muscarinic, and less sensitive to nicotinic, stimulants than the guinea-pig. It is concluded that marked species differences occur in ganglionic transmission.

ELECTROPHYSIOLOGICAL STUDY OF FROXIELL TUBULES OF RAT KIDNEY. G. Bento de Mello and G. Malnic. Dept. of Physiology, Univ. of São Paulo, São Paulo, Brazil.

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Transtubular PD and tubular wall resistances were measured in rat proximal tubules by means of single and double barreled glass microelectrodes. A PD of -2.17 + 0.42 (31 obs) mV, lumen negative, was obtained when tip localization was made by the oil droplet method, and of -4.25 \pm 0.35 (52) mV when made by choline chloride perfusion; both values were significantly different from zero. Specific wall resistance was 14.4 ohm.cm², concordant with a length constant of 139.9 + 11.9 (28) x 10-4 cm. Transfer numbers of 0.47 for Na, 0.40 for K and 6.13 for CI were obtained in microperfusion experiments with changing ionic concentrations; these results were compatible with simultaneous conductance determinations. Luminal and peritubular perfusions with isotonic and hypotonic solutions at different pH indicated the occurrence of streaming potentials of 2 to 7 mV in this structure. Such potentials were of opposite sign and similar magnitude if fluid flow was reversed. Diffusion potentials due to luminal or peritubular perfusion with isotonic solutions of low ion concentration were also approximately symmetrical with respect to the tubular epithelium as a whole. Tubular wall resistance increased significantly upon luminal or peritubular perfusion with hypotonic solutions. These data indicate that there exists an intercellular low resistance path lined with negative fixed charges across the tubular wall, which may be responsible for most of the electrophysiologi cal characteristics of this tubular segment.

CHANGES IN H⁺-ACTIVITY OF MYOCARDIAL INTERSTITIUM IN DOGS DURING LOCAL ISCHEMIA, HYPOXIA, HYPER-AND HYPOCAPNIA. Benzing, H., Gebert, G. Strohm, M., Physiol.Inst., Tübingen and Abt. Physiol., Ulm.

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In 10 mongrel dogs we studied the pH changes in the myocardial interstitium by means of glass microelectrodes(30 - 150 μ diameter, Corning o150 glass). Up to four electrodes were inserted into the left ventricular wall. The potentials were recorded simultaneously against one grounded reference electrode. Further we measured local blood flow by means of heated thermocouples, blood pressure, heart rate, and exspiratory CO2 concentration. Local ischemia was produced by transient occlusion of the left anterior descending coronary artery. In the ischemic region we observed initially a slight alkalosis(0.01-0.05 pH), starting within 15 sec and lasting about 30 sec. Thereafter the pH decreases rapidly by 0.05-0.8 units as a function of occlusion time. After release of blood flow the pH returns to the starting values(occlusion time up to 30 min). -Hypoxia (10% O2) initially causes an alkalosis(0.05 - 0.1 pH), followed by a slow decrease in pH. After returning to normal ventilation, a transient acidosis(0.03 - 0.1 pH)occurs. Hypercapnia(4% CO2) decreases the pH by 0.06 - 0.13 units; hyperventilation(10 min)induces an alkalosis of 0.05 - 0.1 pH.

QUANTITATIVE AND CONTINUOUS INVESTIGATIONS INTO THE KINETICS OF ADP-INDUCED PLATELET AGGREGATION IN DIFFERENT VASCULAR COMPARTMENTS.

Klaus U. Benner and Klaus E. Frede. Institute of Normal and Pathological Physiology, University of Cologne, Germany.

In flowing blood following infusions of adenosine diphosphate (2 x 10^{-2} Mol/1, 1 ml/min) intraarterially or intravenously formation of platelet aggregates can be demonstrated using a recently described photoelectrical technique (Pflügers Arch. 320, 142-151, 1970). When the blood passes the microvascular system of hind leg or lung the number of aggregates is reduced significantly. In the a. tibialis anterior an average of 523.9 \pm 295.3 aggregates and in the v. tibialis anterior an average of 149.4 \pm 187.8 aggregates can be counted in 11 dogs during 10 min of infusion of ADP into the acrta ascendens and another 5 min thereafter. During the same time of infusion and observation but administering ADP into the v. femoralis of 9 dogs an average of 359.2 \pm 197.0 aggregates is counted in blood from the right heart and an average of only 1.9 \pm 2.2 aggregates in blood from the left heart. These decreases suggest a trapping of aggregates in the smallest vessels.

KALLIKREIN CONTENT OF RAT SALIVARY GLANDS DURING DEVELOPMENT. W.T.

Beraldo, Glênio Siqueira, J.A.A. Rodrigues and C.R.S. Machado Departments of Physiology and Morphology, Instituto de Ciências Biológicas, UFMG., C.P.2.486, Belo Horizonte, Brasil.

Beraldo, Araujo e Mares Guia (1966) described an esterase in rat urine that releases kinin fron plasma and causes contraction of rat uterus apparently independent of a substrate present in the uterus. Similar activities were found in rat submandibular gland but a very few if any activities were found in parotid and sublingual glands. In order to investigate the structure where this special kallikrein is found a study of kallikrein concentration during the development of the glands was performed. The kallikrein content increases parallely with the development of the acinar cells. In the newborn submandibular gland contains no kallikrein at all but its production starts after the second week of life reaching its maximum around 70th days. Concentrations equivalent to 200 ug/G bradykinin were found when tested directly on the rat uterus without previous incubation with substrate. Glandular extract also caused fall in rat blood pressure.

This work was supported by grants fron Conselho Nacional de Pesquisas and Conselho de Pesquisas da UFMG.

MEASUREMENT OF ANDROGENS BY GAS-LIQUID CHROMATOGRAPHY IN THE TESTIS OF GUINEA PIG THROU-GHOUT THE FIRST DAY LIFE. M. Berger, G. Pelerdy, A. Robert, N. Rigaudière et P. Delost. Dept. de Physiologie, Complexe Scientifique des Cézeaux, Univ. de Clermont-Ferrand, 63 Aubière, FRANCE.

Testosterone and androstenedione levels in testicular tissue of the newborn guinea-pig are measured every 6 hours throughout the first day of life, using gas-liquid chromatography with tritium electron capture detection. The sensitivity of the method, by means of utilization of heptafluorobutyrate derivative formation, permits the sexual steroids individual dosage. Each lot contains 15 animals. These study indicate: 1) testosterone and androstenedione are present in important quantities in the testis of guinea-pig at birth - 2) with increasing age, there are pronounced variations of these two hormones level in testicular tissue. Concentrations are evaluated in nanogram/100mg wet testicular tissue. The level of testosterone is firstly very high at 0h: $37,2\pm6,7$; it decreases at 6h (18,5 $\pm4,1$), reaching a base line between the age of 6h and 12h (19,8 $\pm3,1$). Then testosterone reaches concentration as low as $12,6\pm2,2$ at 18h. This decrease, constated from 6h, is significant in comparison with 0h; it is about 68% at 18h. At the age of 24 hours a rise in testosterone concentration to $36,7\pm15,1$ is noted. The rate of androstenedione is always lightly lower than this of testosterone; its variations during the first day of life are similar (0h: $33,7\pm8,5$; 6h: $10,4\pm1,6$; 12h: $12,0\pm1,9$; 18h: $10,4\pm1,6$; 24h: $20,7\pm7,0$).

MODIFICATIONS DES MEMBRANES SOUS L'EFFET DE L'ACIDE MALEIQUE AU NIVEAU DU NEPHRON. M. Bergeron, Département de physiologie, Université de Montréal, Montréal, Canada.

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L'acide maléique, injecté par voie intrapéritonéale (9 mM/Kg) chez le Rat, cause une aminoacidurie généralisée et des modifications morphologiques au niveau du tube proximal et distal, intéressant surtout le réseau de membranes périmitochondriales de la base de la cellule. Dès 2 heures après l'injection, les membranes présentent en microscopie électronique une coloration anormalement intense; à 24 heures, on note une disparition de ces membranes. Les membranes intercellulaires, la membrane basale et la membrane apicale (bordure en brosdifiée. A 72 heures, le réseau de membranes se réorganise à la base de la cellule en même temps que disparaît l'aminoacidurie.

Comme nos études de microponction faites chez le Rat in vivo ont démontré que l'acide maléique modifiait la sortie (efflux) plutôt que l'entrée (influx) des acides aminés dans la cellule, l'atteinte membranaire dans ces mêmes conditions pourrait être la cause immédiate du défaut de transport et d'accumulation des acides aminés. Le caractère sélectif et réversible des lésions tant morphologiques que biochimiques confirme le rôle du réseau membranaire périmitochondrial dans le transport de diverses molécules par la cellule rénale.

AN ENTROPY MODEL OF PRIMITIVE NEURAL SYSTEMS. R.M.Bergström, O.Nevanlinna. Inst. of Physiology, University of Helsinki, Finland.

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The purpose of the work is explanation of certain features of the over-all state of the neural system which appears in the sensory physiological situation on the basis of phenomena on cellular level. A simple neural system was so constructed that the total neural energy, defined as the number of impulses circulating in the system, remains constant in the closed system. In accordance with statistical mechanics, an expression is derived for the maximum entropy of the system. The entropy is considered as representing the over-all state of the system. The mean firing frequency takes a similar position in the formalism as the temperature in statistical mechanics. The entropy as a function of the total energy or mean firing frequency is U-shaped. It is zero when the total energy is zero or at its maximum value. Between these points, the entropy has one maximum value. The dependence of the neurons in the system is also derived. The behaviour of the entropy in open systems is studied with the aid of computer simulation. The U-shaped function corresponds to certain empirical findings.

This work has been supported by the Finnish National Research Council.

EFFECT OF FUROSEMIDE ON JUXTAGLOMERULAR INDEX (JGI) AND DISTRIBUTION OF SINGLE GLOMERULAR FILTRATION RATE IN THE RAT. G.Berjal, J-P.Bonvalet, with the technical assistance of M.Champion, F.Wanstok. U2 INSERM, Hôp.L.Bernard, 94, Brévannes, France.

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The effect of furosemide on the intrarenal distribution of single glomerular filtration rate (sgfr) was studied in anaesthetized rats. Sgfr was measured by the 14-C ferrocyanide infusion technique and the JGI was determined. Rats were given iv. furosemide, 5 mg/kg bw. as a prime and 5 mg/kg/hr in saline. Urine losses were replaced by iv. saline (calculated fluid balance:-0.71+0.23 ml).90 min after the prime blood pressure (BP) was:107+3 S.E.mmikg, urine flow (V):76+17 µ1/min/kidney,Cin:0.768+0.104 ml/min/kidney (control periods, BP:100+6 V:2.9+0.7,Cin:1.018+0.098),Uosm:354+17 mOsm/1,UNa:135+3 mEq/1. In four kidneys the JGI was markedly reduced (9+3),sgfr's were 39.6+2.79 and 41.9+3.25 nl/min for superficial (S) and juxtamedullary (JM) nephrons,respectively,sgfrs/sgfn/M being0.972+0.043. In one kidney JGI was not reduced (39),sgfr's were S:32.4+4.0,JM:48.5+3.0 nl/min,S/JM:0.668,values similar to nondiuretic normal rats (n=10,sgfrs:32.7+1.4,sgfr/M:41.1+1.9 nl/min,JGI:36+9). The results show that during furosemide diuresis sgfrS becomes equal to sgfr/M, once JGI sharply decreases. This confirms previous results obtained with similar techniques in nondiuretic and salt-loaded rats, suggesting that sgfr and granularity of the juxtaglomerular apparatus (JGA) are inversely related. The fact that under conditions of increased Na-load at the macula densa a degranulation and a redistribution in snfr of the kidney simultaneously occurs seems to support the idea on the role of this Na-load in the regulation of sgfr, nephron by nephron, via their own JGA.

PLASMA FREE FATTY ACID LEVELS IN PAPUA PENGUINS. J. Bernaldez and J.C. Roche. Argentine Antarctic Institute, Buenos Aires, Argentina.

Plasma free fatty acid levels in papua penguins were studied at the Scientific Station Almirante Brown, located in the Antarctic Peninsula (Lat. 64° 53 S, long. 62° 55 W). The experiment was designed to study the effect of: (1) seasonal variations; (2) starvation. (3) glucose loading and (4) norepinephrine and A.C.T.H. injection. Seasonal variations occurred. Maximum F.F.A. levels were observed in winter time (May 539^{\pm} 50.3 μ M/L.; April 508^{\pm} 31.5 μ M/L.; October 541^{\pm} 26 μ M/L.). Minimum levels were registered in summer time (March 379 μ 31 μ M/L.; December 279 μ 17 M/L.). Penguins unlike mammals and other avian species showed diminished plasma F.F.A. levels (Fed: 520^{\pm} 25 μ M/L.; fast: 1st. day 528^{\pm} 24 μ M/L., 3rd. day 340^{\pm} 42 μ M/L., 7th. day 380^{\pm} 42 μ M/L., 11th. day 376^{\pm} 38 μ M/L., 16th. day 201^{\pm} 35 μ M/L.). Glucose loading resulted in a decrease of F.F.A. levels. Norepinephrine and A.C.T.H. injection increased F.F.A. The physiological tinding on F.F.A. in papua penguins dittering from mammals and other avian species will be discussed.

161 RELATIONS OF MEMBRANE POTENTIAL AND CURRENT CHANGES TO CONTRACTION IN ISOLATED TWITCH MUSCLE FIBRES. Cl. Berhard. Laboratory of Animal Physiology, CNRS-ERA n°111, 86 Poitiers, FRANCE.

Membrane currents during depolarization steps were determined by the double sucrose-gap technique and simultaneous contractile responses were measured by a microphotoelectrical method.

The record of the contractile tension was based on the measurement of the transmitted light variations associated to the movement of the single fibre on a small area in the central experimental compartment of the double sucrose-gap system where the membrane potential was clamped. The time-constant of the whole device was shorter than $50~\mu s$.

In Ringer solution the relation between contraction and membrane potential was sigmoid. Contractile responses started at -45 mV and reached a maximum at about -20 mV. No direct relation between membrane current and contraction amplitudes could be observed in these preliminary experiments.

162 CONTROL OF RESPIRATION BY MEDULLARY EXTRACELLULAR pH. J. Berndt and W. Berger. Inst. für Physiologie, Ruhr - Universität, Bochum, Germany.

In the peripherally chemodenervated cat (carotid nerves interrupted), respiratory responses can still be elicited by varying either blood or cerebrospinal fluid acid-base parameters. These responses are attributed to chemosensitive structures located near the ventral surface of the medulla. By application of a mathematical model of bicarbonate and carbon dioxide diffusion in brain tissue to experimental data it can be demonstrated that the respiratory response to a change in either arterial carbon dioxide tension or CSF hydrogen ion concentration is a unique function of medullary extracellular pH at a distance less than 1 mm from the ventral surface. This is considered to confirm the hypothesis of a superficial localization of the chemosensitive structures which therefore are very probably not identical with the classical respiratory centres. In the decerebrate cat, the sensitivity of these structures (central chemoreceptors) allows doubling or trebling of resting ventilation when the medullary extracellular pH changes from 7.3 to 7.2 . In the anesthetized animal (chloralose - urethane) mainly the tidal volume and only slightly the respiratory frequency contribute to the ventilatory responses to changes in medullary extracellular pH if the vagal nerves are intact. Vagotomy abolishes the frequency response while the total ventilatory response remains unaffected.

FREQUENCY ANALYSIS OF VESTIBULAR INFLUENCE ON NECK AND FORELIMB EXTENSOR MOTONEURONES IN THE Minneapolis, Minn. 55455 U.S.A. Lab. of Neurophysiology, Univ. of Minnesota,

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Decerebrate cats with spinal transection at T 12 level were subjected to whole body, sinusoldal or triangular, low frequency (.1 to 2 Hz) rotations, around longitudinal (X), transverse (Y) and vertical (Z) axis, at peak to peak velocities ranging from 10 to 100°/sec. Single, or groups of motor units activity was recorded by EMG of neck extensor and triceps muscle. A Modulation of Motor Unit Frequency (MMUF) was observed during rotation, it was shown to be of vestibular origin. For MMUF related linearly to stimulation, the gain and phase between applied computer. During X axis rotation, the gain drops by about 10 dB from .1 Hz to 1 Hz for constant velocity input. The phase is constant over the frequency range studied and is slightly lagging labyrinthectomy: the contralateral triceps MMUF was then lagging acceleration of input oscillation by about 30° (90° phase advance). In both normal and hemilabyrinthectomised cats motoneurone activity of neck extensors was in phase with the contralateral triceps. MMUF was also measured during Y and Z axis rotation. This study shows how, within physiological range, overall vestibular dynamic control on neck and limb extensors is related to velocity of movement.

FIRING PATTERN OF PNEUMOTAXIC CELLS. F. Bertrand and A. Hugelin. Lab. Physiology, U.E.R. Saint-Antoine, 27 rue Chaligny, Paris 12°, France.

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Localization of the pneumotaxic system in the nucleus parabrachialis medialis (NPBM) at the level of the upper pons is supported by 3 types of experimental evidences: 1) apneusis production by electrolytic lesions restricted to 1/50 th of the NPBM; 2) observation of more than 90 percent of respiratory cells in the NPBM; 3) synchronization of respiration by NPBM single shock stimulation. A study of the spatial distribution of 1.000 respiratory cells and of their phase relation with phrenic discharge lead to the conclusion that 3 self re-exciting systems are located inside the NPBM.

FEEDING RHYTHM RESPONSES TO SHORT DAY PHOTOPERIODS (SDP). E. L. Besch and C. L. Chen. Dept. of Physiol. Sci., Col. of Vet. Med., Kansas State Univ., Manhattan, Ks. 66502.

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Male, Sprague-Dawley rats, 200-300 grams in weight and 12 per group were exposed, in series, in a controlled environment room to control days (12L:12D) and SDP (2L:2D). In one experiment, temperature was cycled — periods of warm (27 \pm 1°C) and light followed by equal length periods of cool (16 \pm 1°C) and dark — and in the other experiment held constant at 21.5°C. In both cases, a 4-hour exogenous rhythm was superpositioned upon the free-running circadian rhythm following exposure to SDP from control days indicating that food intake is influenced to a greater extent by photoperiod than temperature. Moreover, the amount of feed consumed did not vary significantly between control and SDP rats in absolute amount or relative intake during any of the dark or light periods. In the third experiment, those rats born and raised under SDP (F₁ generation) and constant temperature displayed no circadian food intake pattern during 2L:2D, only a 4-hour rhythm. Although these F₁ pups had apparently larger birth weights, their food and water intake do not appear to be significantly greater than control animals. These data suggest that SDP has a significant effect on the food intake rhythm in rats and that this rhythm may be entrained by a short day photoperiod.

(Funded by USAFOSR Contract No. F44620-68-C-0020).

NET CURRENTS AND CONDUCTANCES IN FROG ATRIAL FIBRES. VOLTAGE AND TIME DEPENDENCE ANALYSIS ACCORDING TO THE HODGKIN-HUXLEY EQUATIONS. A. Besseau and Y.M. Gargoutl. Laboratory of Animal Physiology, CNRS-ERA 111, 86-Poitiers, FRANCE.

In frog atrial fibres, investigated by the voltage-clamp technique, each of the net membrane ionic currents can be obtained using specific inhibitors and/or modified solutions. Thus, an initial fast inward Na⁺-current, a slow inward Na⁺-Ca+-current and an outward K⁺-current have been dissociated from the total current and corrected for capacitive and leak components. An attempt has also been made for separating the Na⁺ and Ca⁺⁺components from the total slow current. Time constants concerning the rate of rise and the inactivation phases at different potentials have been measured for each current. Weak depolarization and hyperpolarization steps have been especially studied. The voltage or time-dependent parameters defined by HODGKIN and HUXLEY have been used to explain the voltage-dependent time course of currents. The equilibrium potential values have been estimated and conductance curves drawn. The relation between the action potential and the currents has been established. The most important feature is the very long inactivation time constant of the slow inward current at the plateau potential range. This slow inactivation phase could be due to the Na⁺fraction of the slow current and could partially account for the long-lasting plateau in frog myocardium. A comparatively important outward current is then necessary to overcome the inward depolarizing current and to repolarize the membrane.

167 EFFECTS OF ORBITAL GYRUS ON INTERNEURONS IN THE CAT DORSAL HORN. J.M. Besson M.C. Maillard, C. Conseiller and P. Aléonard. Physiologie des Centres Nerveux - Faculté des Sciences, Paris, FRANCE.

The orbital gyrus exerts a powerful inhibitory action on different types of reflexes at various levels of the CNS. Concerning the nature of this inhibition, postsynaptic mechanisms were described by Nakamura et al (Brain Res, 6, 184-198, 1969) on the masseteric monosynaptic reflex, but this modality is certainly not the only one since dorsal root potentials were obtained by orbital gyrus stimulation (Abdelmoumène et al., Brain Res, 20, 327-329,1970). The present investigation is devoted to the effects of orbital gyrus stimulation on the interneurons of Rexed's laminae IV and V in the cat lumbar dorsal horn. Cells were characterized by their location, but chiefly by their dorsal horn. Cells were characterized by their location, but chiefly by their the observation of 175 cells, it results that the inhibitory effect is prominent since it was found on 83% of cells in Layer IV and on 60% of cells in Layer V. There is a good correlation between the time course of the inhibitory effect and the time course of dorsal root potentials induced by orbital stimulation. The meximal effects on the increase of latency and on the suppression of the number of spikes of the test response were found approximatively for an interval of 35 ms between cortical and peripheral stimulation. The duration of the inhibitory effect is of the order of 150 ms.

168 EFFECTS OF DRUGS ON THE IN VIVO RELEASE OF NEWLY SYNTHETIZED H3 DOPAMINE (H3DA) FROM H3 TYROSINE IN THE CAT CAUDATE NUCLEUS. M.J. BESSON, A. CHERAMY, P. FELTZ, J. GLOWINSKI. Groupe de Neuropharmacologie biochimique, Collège de France, PARIS.

The spontaneous and pharmacologically induced release of H3DA has been studied using a cup technique which allowed a continuous superfusion of a limitated area of the ventricular surface of the caudate nucleus with H3 tyrosine. Superfusates were collected in serial fraction and analyzed for their H3DA content.

1) In the unanesthetized cat immobilized with flaxedil, H3DA released spontaneously in a resting state situation was identified and estimated quantitatively in collected fractions. The spontaneous release was decrease by 65% with tetrodotoxin application.

2) Marked and rapid increase in the release of H3DA (5 to 10 times the resting release) has been induced respectively by topical application of K_+ , Catron and d-amphetamine. Both, d and 1 amphetamine enhanced H3DA release when injected i.v.

3) Acetyl choline applied topically, inhibited the spontaneous release of H3DA, this effect was blocked by atropine.

THE RENIN ANGIOTENSIN SYSTEM IN THE CHRONICALLY RENAL ALLOTRANSPLANTED HUMAN. J. Best, J. Anderton, P. Kincaid-Smith, R. Yu. Dept. of Medicine, Monash University/University of Melbourne, Melbourne, Vic., Australia.

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The aim was to examine the renin-angiotensin system in subjects with a well-established renal transplant. Thirty-three subjects were studied of which fourteen had renal artery stenosis to the transplanted kidney disclosed by arteriography. Levels of plasma renin activity (PRA), plasma renin concentration (PRC) and plasma renin substrate (PRS) were measured by the method of Skinner (1967) and blood angiotensin II (AII) was measured by a method modified from that of Catt, Cain & Coghlan (1968). Levels of PRA, PRC, PRS and blood AII in all subjects with chronic transplants were significantly higher than those obtained in normal subjects, and all levels were raised significantly further if renal artery stenosis was present to the transplanted kidney. Whereas in the presence of a normal renal artery the levels of PRA correlated significantly with blood AII (r=0.613 p<0.01), this correlation was no longer significant in the presence of renal artery stenosis, the levels of PRA appearing disproportionately greater than the values of blood AII. The conclusion suggested is that there is a factor interfering with the formation of blood angiotensin II either directly inhibiting plasma renin activity in vivo or preventing the conversion of angiotensin I to angiotensin II.

ENERGETIC POTENTIAL OF CEREBRAL CORTEX AND EEG, CSF-Na $^+$, K $^+$ DURING HIGH CO $_2$ -CONCENTRATION IN AMBIENT AIR. E. Betz, H. Pfeiffer, M. Strohm. Physiolog. Institut, Tübingen.

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In anaesthetized cats exposed to 50-80 % CO₂ the EEG disappears. Exposure of 1 h to CO₂ causes postsynaptic dendritic swelling as seen with electron-microscopy. The cortical ATP increases to more than 2 'u M/g fresh tissue (normal 1,6-1,9 'u Mol/g) as well as the ATP/ADP. The Cr-P/Cr decreases from the average of 0,46 to 0,25 (normal 0,46). The lactate content of the tissue rises (from 1,83 to 3,75-5,27) and also the lactate / pyruvate (20 to more than 70). Changing blood pH by infusion of NaHCO₃ during high CO₂ causes only slight increases of the CSF-pH despite normalisation of the blood pH. ATP is higher than in acidosis whereas Kr-P is like in pure acidosis. The EEG remains ceased infusions of TRIS causes also increases of ATP/ADP and decreases of Cr-Ph-/Kr. Fall of systemic blood pressure beyond 70 mm Hg causes a simultaneous decrease of the energy rich phosphates in all cases.

CSF-K⁺ increases, CSF-Na⁺ and blood-K⁺ rise slightly.

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FUNCTIONAL ORGANIZATION OF THE MEDIA OF A MUSCULAR ARTERY. J.A. Bevan, C. Su, J.G. Waterson. Dept. of Pharmacology, UCLA Sch. of Med. Los Angeles, Calif. USA.

Spontaneous and induced contractile characteristics of the isolated ear artery of the rabbit have been studied in vitro to delineate the functional organization of its vascular muscle components. Small amplitude, eous, phasic contractile movement was observed on recording longitudinal tension, but not perfusion resistance of the intact vessel. This has the characteristics of propagated multifocal, asynchronous activity. Rate and amplitude were influenced by stretching the vessel. It was obliterated by longitudinal or helical section. Propagation of excitation appeared to occur also in the radial axis within the vessel wall in either a centrifugal or centripetal direction. A transient propagated response was triggered by exposure to some vasoactive drugs for only 1-2 secs. The magnitude of this response was dependent not so much upon the time as on the concentration of drug exposure. Upon longer exposure, a secondary tonic contraction reminiscent of that seen in elastic vessels e.g. thoracic aorta occurred. Propagation of contraction also took place in the longitudinal axis of the vessel, probably along a helical course. Contrasting models of smooth muscle cell organization in muscular and elastic arteries will be proposed. Supported by USPHS, LACHA, AMAERF.

- TENSION STUDIES IN VOLTAGE CLAMPED FROG SKELETAL MUSCLE. F. Bezanilla and C.Caputo, Dept. of Physiology, Univ. of Rochester, Rochester, N.Y., U.S.A. 172 Fibers 1.5 to 2 mm long were dissected in small bundles from the Lumbricalis muscles of the frog. The space constant of these fibers is approximately 2 mm and, due to their short length, current injected through an electrode in their center produces a fairly uniform voltage (V) deflection along the fiber for sufficiently long pulses. For voltage clamping, another electrode was inserted very close to the first one to measure V. Conventional feedback circuitry was employed. Tension was measured with an RCA 5734 transducer. The experiments were carried out at 12°C in Ringer's solution with 10°C g/ml TTX added. The relation between peak tension and the amplitude of depolarizing pulses could be described by an S-shaped curve. A family of such curves was obtained employing pulses of different duration. As the pulse duration was increased, the threshold decreased, the maximum tension increased and in most cases the maximum slope of the curves increased. Double pulse experiments were carried out, in which a subthreshold prepulse of 100 msec. preceded a larger pulse of 10 msec. The amplitude of the second pulse was such that by itself it caused a very small tension. When the prepulse immediately preceded the pulse the tension developed by the fiber was much increased. Supported by USPHS NS 08893 01.
- CONTRACTILITY OF ISOLATED ATRIAL MUSCLE OF ENDOTOXIN-TREATED GUINEA-PIG. B. Bhagat,
 Michael Beaumont, M. W. Rana, M. S. Ellert, and D. Cavanagh, Department of Physiology,
 St. Louis University School of Medicine, St. Louis, Missouri, U.S.A.

In endotoxin-treated left atrial strips the contractile force developed at standard resting tension was significantly lower than that in control. Similarily, the contractile force developed in endotoxic strips was significantly lower than that of control at all frequencies applied. Coupled pacing and histamine augmented the force in both (normal and endotoxin group) to the same degree, but absolute contractile force was lower in the endotoxin group. Since reduced sodium or potassium ion concentration in the medium caused a significantly lower shift of the frequency-contractile force curve in the endotoxin group, it is suggested that endotoxin exerts an influence on the active transport process of cardiac cell membrane. On the other hand, an increase in extracellular calcium caused enhancement of contractile force to an equal degree in experimental and control groups. This suggests that endotoxin treatment exerts an effect on storage and/or mobilization of calcium ions, resulting in decreased availability of calcium for the contractile process. Thus, it is concluded that the defect for generating contractile force by endotoxic heart may lie somewhere within the events which link the process of excitation and contraction.

SEROSAL AND MUCOSAL PERMEABILITY COEFFICIENTS IN TURTLE AND RAT ISOLATED JEJUNUM. A. Bianchi, F. Repetto, B. Giordana and V. Capraro. Inst. of General Physiology, University of Milan, Milan (Italy).

Washout fluxes in the isolated jejunum of Testudo graeca, preloaded with thiourea, show a passive permeability of the serosal membrane $(P_{\rm S})$ higher than the mucosal one $(P_{\rm m})$, the $P_{\rm S}/P_{\rm m}$ ratio being 1.43 (Lippe C. et al., Arch. Int. Physiol. Biochem. 73, 43 (1965)). The same result $(P_{\rm S}/P_{\rm m}=1.57)$ occurs when the permeability coefficients are calculated by measuring the steady state concentration differences between cell and mucosal as well as serosal side. Conversely the $P_{\rm S}/P_{\rm m}$ value for acetamide in isolated rat jejunum evaluated by means of the latter technique is reversed $(P_{\rm S}/P_{\rm m}=0.18)$ (Esposito G. et al., Proc. Int. Conf. Biol. Membr. 1969, p.74). These different passive permeability ratios in rat and turtle jejunum can be attributed either to species permeability differences referred to surface unity or to a different development of mucosal and serosal membranes in the two species.

In order to test the latter hypothesis intestinal preparations are examined by electron microscope.

NEURONES RESPIRATOIRES BULBAIRES ET REGULATION DE LA RESPIRATION. A.L. Bianchi, D. Planche et M. Dussardier. Lab. Physiologie générale, Faculté des Sciences, Centre de Saint-Jérôme 13 - MARSEILLE 13e - FRANCE.

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Chez le Chat anesthésié, la réception par microélectrode permet de différencier trois populations de neurones bulbaires ayant manifestement des fonctions différentes : des neurones bulbo-spinaux (54 p. cent) que l'on peut activer par stimulation antidromique de la moelle épinière, et qui constituent l'étage de sortie des centres de commande bulbaires, des motoneurones vagaux (4 p. cent) qui constituent un étage d'exécution, des neurones propriobulbaires (42 p. cent) qui ont vraisemblablement un axone court compris tout entier dans le bulbe. Lorsque la décharge de ces neurones est modifiée soit par stimulation du cortex cérébral, soit par mise en jeu des afférences vagales, on constate que chaque catégorie anatomo-fonctionnelle répond d'une manière qui lui est propre. Par exemple la stimulation corticale arrête transitoirement la décharge des neurones propriobulbaires ; au niveau des neurones bulbo-spinaux on observe en outre une brève activation. Le point d'impact des facteurs de régulation peut donc être précisé en tenant compte des différents étages fonctionnels constituant le centre respiratoire bulbaire.

AN INDICATOR-DILUTION TECHNIQUE FOR STUDYING ERYTHROCYTE AND PLASMA FLOWS AND VOLUMES IN THE INTESTINAL MUCOSA-SUBMUCOSA OF THE CAT. B. Biber, O. Lundgren and J. Svanvik. Dept. of Physiology, Univ. of Göteborg, Sweden.

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An indicator-dilution technique using nondiffusable intravascular tracers is developed. A Geiger-Möller tube is placed in close contact with the intestinal mucosa. Known amounts of radioactive tracers are "instantaneously" administered intraarterially while total intestinal blood flow is continuously and directly recorded. Using erythrocytes and colloid "plasma" particles, both labelled with ³²P, erythrocyte and plasma flows were separately calculated from the maximal height of the recorded curves, the arterial hematocrit, the total blood flow and the injected amount of tracer. These factors, together with the area under the curves, also give the regional erythrocyte and plasma volumes. Due to the weak penetration of the ³²P radiation, the luminal detector will only "see" the mucosa-submucosa. – During "rest" (total intestinal blood flow 29 ml/min x 100 g) the mucosal-submucosal blood flow and blood volume were estimated to 20 ml/min x 100 ml tissue and 2.3 ml/100 ml tissue. The calculated hematocrit in the monitored region was 77 % of that in arterial blood (p < 0.01). At intense vasodilatation (total intestinal blood flow 200 ml) the corresponding figures were 190 ml and 4.2 ml. During neurogenic vasoconstriction the mucosa-submucosa flow was less affected than the total intestinal flow.

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CHANGES IN BRAIN TISSUE OXYGENATION DURING ACUTE HYPOGLYCEMIA AS DETERMINED WITH OXYGEN.ULTRAMICRO-ELECTRODES AND ON LINE COMPUTER SIMULATION. H. I. Bicher, D. D. Reneau, D. F. Bruley and M. H. Knisely. Dept. of Anatomy Medical University of South Carolina, Charleston, South Carolina 29401, USA.

Brain tissue PO₂ and neuronal action potentials are determined simultaneously from the 14 tip of an oxygen electrode. Concomitantly blood flow, blood pressure and arterial PO₂ are measured. The "reoxygenation time" (period of time needed to resupply a microarea of brain tissue after a short period of anoxic anoxia) is used for the determination of the overall ability of the circulation to carry oxygen to the brain. During acute hypoglycemia blood flow is increased, the "reoxygenation time" shortened, but the normal electrical response of the neurons is impaired. Analog computer simulation performed on line were able to predict the tissue PO₂ changes, thus confirming the reliability of the equations used.

Supported by the 1971 state of South Carolina appropriation for research and NIH Grants NB-08228, NB-06957, HE-04176 and HE-05340.

178 FUNCTIONALLY DISTINCT AREAS IN THE CUNEATE NUCLEUS OF THE RHESUS MONKEY. M.A.Biedenbach & A.L.Towe. Dept. of Physiol., Univ. of Wash., Seattle, Wash. 98105, U.S.A.

Neurophysiological and histological methods were used to reveal if different functional areas in the cuneate nucleus exist and if they have distinct morphological properties. All areas within the nucleus were systematically searched with a microelectrode for unit poten-For each unit found, the exact location and a set of response properties (receptive field size, stimulus modality, cortical excitation or inhibition, etc.) were recorded. Spatial distribution maps of all units and of several unit subsets (each with different response properties) were made. Histologic sections were prepared from a block of brain tissue matching that investigated with the microelectrode. Camera Lucida drawings of the borders of the nucleus and of each neuron within were obtained, then distributions of all cells and of cell subgroups plotted. Maps of all unit potentials and of all cells were highly correlated, showing units were recorded in proportion to cell density. Unit and cell subgroups were distributed coextensively, but certain subgroups showed preferred spatial distributions, e.g., in the caudal part of the nucleus, polygonal cells, units with large receptive fields, and cortically excited units make up greater fractions of the local population than they do in the rostral part. Other subgroups, e.g., touch units, seemed more evenly distributed, but testing for additional response properties revealed that touch units with a highly convergent input from periphery or cortex were more numerous in the caudal than in the rostral part of the nucleus. Thus, input distributed evenly may get processed differently in different areas. (Supported by USPHS grants NS00396 & NS005136)

179 MOVEMENT DETECTORS ON THE PIGEON'S OFFIC TECTUM. M.Bilge. Department of Physiology and Biophysics, Cerrahpasa Faculty of Medicine, University of Istanbul, TURKEY.

In the "stratum griseum centrale" of pigeon's optic tectum we have recorded action potentials of three types of units, evoked by moving visual stimuli, moved across the respective receptive fields. These units are: 1. Movement detectors, 2. Directional movement detectors, 3. Acceleration detectors. These units are not sensitive to the stationary stimuli (i.e., to on and off of a stationary light spot). The receptive fields of the unit type 1. and 2. are strictly rectangular, long axes of which are oriented vertically or horizontally. None is found in an oblique orientation. Another characteristic feature of these rectangular receptive fields is that they are mostly (70%) bordered by the horizontal meridian. This may have some significance in the very important mechanism of the visual orientation of the birds during the flight. Unit type 3. is almost not sensitive to linear movements of visual stimuli, but it can be activated only by complex movements of small objects (i.e. acceleration and deceleration) across the wery large receptive fields with ill defined borders. This latter type of unit is much more common in the "nucleus isthmi" than it is in the "st.griseum centrale" of the tectal cortex. Other two additional unit types in the "nucleus isthmi" are: 4. Movement detectors with quick habituation, and 5. Acceleration detectors with considerable after discharge.

SERUM NA CONCENTRATION AND RENIN SECRETION. Adil Birbari, Department of Physiology, American University of Beirut, LEBANON.

Following infusion of 0.5 ml of 5% saline to a group of 10 Sprague-Dawley female rats over one hour, the mean plasma renin activity (PRA) was 640 + 58.15 ng/100 ml; the mean serum Na and blood volume were $203.9\overline{0} + 3.09$ mEq/1 and 7.4 ml/100 gm body weight respectively. In a control group, the mean respective values were: 1220 + 55.41 ng/100 ml (p<0.001), 166.30 + 3.86 mEq/1 (p<0.001) and 7.38 + 0.31 ml/100 gm body weight (p>0.1). In a third group of female rats, peritoneal dialysis with 25 ml of 5% dextrose was performed for 3 hours, the mean serum Na dropped to 146.2 + 4.76 mEq/1, while the mean PRA rose to 2450 + 233.62 ng/100 ml (p<0.001 for both values); the mean blood volume was 7.86 + 0.22 ml/100 gm body weight (p>0.1). These results suggest that the serum Na concentration may play a role in the control of renin secretion.

CAPILLARY FILTRATION RATE IN CAT HIND LIMB MUSCLES DURING HAEMORRHAGE.

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To clarify the changes occuring at capillary level during haemorrhagic hypotension and shock the capillary filtration coefficient/CFC/ in cats anesthetized with Chloralose-Uretane was measured according to Mellander et al./Circ.Res. 13:105-118,1963/. It was found that: /l/ neither 60 nor 120 min haemorrhage to 50-60 mmHg level caused significant changes in CFC, /2/ when a 3 hour duration two-step haemorrhage was performed, 90 min at 60 and 90 min at 40 mmHg level, the CFC values decreased to about 40% of the initial level in the second period and this reduction remained unchanged after reinfusion of the whole blood, /3/ Butylsympathon, a shock-protecting drug significantly increased the CFC values above the control level in normal cats. It is supposed that the shock protecting effect of several drugs might be explained by their direct action on the capillary wall increasing the capillary filtration and thus preventing the irreversible changes of microcirculation during shock.

INHIBITION AND POTENTIATION OF MECHANICALLY AND ELECTRICALLY ELICITED MONOSYNAPTIC REFLEXES DURING AND AFTER TENDON VIBRATION. Beverly Bishop, Richard Johnston and Corrine Scoville. Department of Physiology, State University of New York at Buffalo and Department of PM&R, Veterans Administration Hospital, Buffalo, New York 1h2lh, U.S.A.

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Application of mechanical vibration to a muscle or its tendon is known to excite selectively the primary endings of the muscle spindles, thereby inducing a weak but sustained tonic contraction. During such application of vibration to the Achilles tendon of man (50 Hz for 100 sec.) the monosynaptic reflex elicited by tendon tap or by electric shock (H-Response), shows a marked or total depression, even in subjects who exhibit no tonic contraction. The equivalent suppression of the spindle-dependent and spindle-independent reflexes with or without a tonic contraction suggests that the inhibition is not only central but presynaptic. However, immediately following the termination of vibration the tendon tap reflex is dramatically potentiated while the H-Response remains depressed for 100 sec. or more. This potentiation of the spindle-dependent reflex suggests that mechanical vibration augments the dynamic sensitivity of the muscle spindles.

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ULTRASTRUCTURAL AND ENZYMATIC CORRELATIONS IN MATURING RABBIT RETICULOCYTES. Charles Bishop and Bahram Parsa. Depts. of Pathology and Medicine, State Univ. of New York at Buffalo, Buffalo, N.Y. 14214, U.S.A.

To better understand the relationship between structure and metabolism, rabbit erythrocytes were separated by ultracentrifugation on albumin density gradients. Density layers were graded according to their content of reticulocytes of Type I (extensive reticulum), II (intermediate), and III (sparse). Layers were also examined by electron microscopy and were assayed for glucose-6-phosphate-, 6-phosphogluconate-, and isocitrate dehydrogenases, and hexokinase, and glutamate-oxalacetate transaminase. Lightest layers had the most Type I reticulocytes, whose mitochondria were best developed, and these layers generally had highest enzyme activities. Increasingly heavier layers contained fewer Type I reticulocytes, less-distinct mitochondria in the reticulocytes, and lower enzyme activities. Bleeding to enhance reticulocytosis gave rise to additional layers of red cells that were lighter than normal but the pattern of morphological and biochemical changes was similar except shifted. Reticulocytosis by phenylhydrazine injection produced quite irregular patterns. Despite the irregularities, those layers with more of the younger reticulocytes generally had higher enzyme activities. These results suggest that the higher enzyme activities of young reticulocytes are associated with the presence of certain structural elements such as well-developed mitochondria. (Based on Ph.D. Thesis submitted to SUNYAB by B. Parsa)

PICROTOXIN, BICUCULLINE AND INHIBITION IN THE CEREBELLAR CORTEX.

S. Bisti, G. Iosif and P. Strata. Institute of Physiology, University of Pisa and Laboratory of Neurophysiology of the CNR, Pisa, Italy.

Two types of postsynaptic inhibition exist in the cerebellar cortex: one exerted by the basket cells and the other by the Golgi cells. They were tested in nembutalized, curarized, intact cats by coupling stimulation of the parallel fibres with a later cortical field response to white matter stimulation. The basket inhibition was inferred from the reduction in size of the antidromic field component of the response, and the Golgi inhibition from the reduction in size of the field generated by the axon discharge of the granule cells. Both inhibitions were suppressed after the systemic administration of picrotoxin (2-5 mg/kg) or bicucul line (0.2 mg/kg). Considering the known antagonism between these substances and the inhibition induced by the χ -aminobutyric acid, the hypothesis is favoured that both kinds of cerebellar inhibitions are mediated by this amino acid.

185 SOME FEATURES OF CORTICO-HYPOTHALAMO-RETICULAR CONTROL IN AUTONOMIC HOMEG-STASIS. E.Bittman and N.Răiciulescu. Inst.of Normal and Pathological Physiology "D.Danielopolu", Academy of Medical Sciences, Bucharest, Romania.

In 110 dogs and 46 cats the authors investigated: 1. the tensional changes which take place in simultaneous activation of cortical and subcortical vasomotor projections; 2. the influence of the midbrain reticular formation (MRF) on some sympathetic and parasympathetic reflexes (sinocarotid baroceptive reflexes, vesico-constrictor reflex); 3. the influence on the electrocardiogram of various areas of the hypothalamus and MRF. The results obtained are indicative of complex relations between the higher nervous centres involved in autonomic homeostasis control. Attention must be focussed at least on the following evidences: 1. the occurrance of spatial summation phenomena after subliminal simultaneous stimulation of some vasopressor or cardiomotor points in the CNS; 2. some findings suggest a differential activation of bulbar areas; 3. the minimal electric stimulation seems to disclose the intrinsic tonic action of the MRF on the explored autonomic reflexes; 4. MRF exhibits influences of the reciprocal innervation type on the autonomic reflexes.

EFFECT OF LITHIUM AND BARIUM IONS ON ACETYLCHOLINE RELEASE FROM THE CEREBRAL CORTEX. M.Bjegović and M.Randić.Laboratory of Neuropharmacology, Institute "Rudjer Bosković", Zagreb, Yugoslavia.

Many investigators have shown that there is a continous release of acetylcholine /ACh/ from the cerebral cortex in amounts which can be directly related to the level of cortical activity. It is believed that ions play a vital role in this process. In our experiments the influence of some ionic changes in Ringer-Locke solution on the spontaneous and evoked release of ACh from the cerebral cortex was studied. Experiments were done in cats anaesthetized with Dial using "Perspex" chamber technique. When the effects of barium ions were studied, calcium was omitted and replaced with equimolar concetration of barium chloride. Preliminary results point out to a significant increase /about 102%/ in the spontaneous release of ACh in barium-Ringer solution, but there was no usual increase in ACh output during peripheral stimulation. In ten experiments sodium chloride of the Ringer-Locke solution was replaced by lithium chloride. The spontaneous release of ACh remained unchanged, but there was no increase in the output of ACh during peripheral stimulation. This depressing effect of lithium ions on the evoked release of ACh from the cerebral cortex was readily reversed by restoring sodium to the collecting fluid.

DYNAMICS OF ARTERIAL OXYGEN TENSION IN RESPONSE TO SINUSOIDAL WORK LOAD IN MAN. H. Bjurstedt and O. Wigertz. Dept. of Physiology and Medical Physics, Karolinska Institutet, Stockholm, Sweden.

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Dynamic characteristics of the response of arterial 0_2 tension (P_{aO}) to supine submaximal leg exercise were studied in 7 physically active young men. P_{aO} was recorded continuously in the radial artery at the wrist; work load was varied sinusdially between the extremes of 250 and 1050 kpm/min with periods of 0.75, 1.5, 3.0, and 7.0 min. Time-averaging harmonic analysis showed a clear dominance of the fundamental component over the second and third harmonics in the P_{aO} response, indicating approximately linear properties of the underlying system within the work-load region studied. Referring P_{aO} changes to blood entering the left heart, the dynamic P_{aO} /work-load transfer relationship could be described by a second-order transfer function with a marked resonance peak in amplitude for periods near 3.0 min (peak-to-peak deviations approaching 14 mm Hg) and an estimated pure time delay of 15 sec. The transfer function for P_{aO} , suggestive of a controlled behavior of this variable, indicates that the basic response of P_{aO} to a change in work load is a change in the opposite direction. The existence of a resonance is interpreted in terms of an unbalance between factors determining 0_2 uptake from, and supply to, the alveolar space.

ALDOSTERONE CONTROL - A FIFTH FACTOR? J.R. Blair-West, J.P. Coghlan, D.A. Denton, and B.A. Scoggins. Howard Florey Laboratories of Experimental Physiology - University of Melbourne, Parkville, Victoria, 3052, Australia.

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It is established that four factors - increased concentration of $K^{+},$ angiotensin, and ACTH, and decreased concentration of Na* in the plasma directly stimulate the secretion of aldosterone by the adrenal gland. The corticosteroid secretion of the autotransplanted adrenal gland of Na* deficient conscious sheep has been studied following the consummatory act of satiation of salt appetite by rapid drinking of 2-3 l of 300 m Eq/l NaHCO3 solution. Many animals show a reproducible large evanescent fall of aldosterone secretion not accounted for by change in any of the four factors listed above. The data is consistent with other evidence on an unidentified factor(s) in aldosterone control.

ELASTICITY MEASUREMENTS OF FROG AND RAT SKELETAL MUSCLE IN ORDER TO ESTIMATE SOME PARAMETERS OF A SLIDING FILAMENTS MODEL. T. Blangé,

J.M. Karemaker and A.E.J.L. Kramer. Dept. of Physiology and Dept. of Med. Physics, Univ. of Amsterdam, The Netherlands.

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The elasticity of isometric tetanized frog sartorius and rat anterior gracilis muscle was measured using quick shortening and quick stretch techniques. Displacements could be imposed within such a short time (0.1-0.3 msec) that little or no influence of detachment and attachment of crossbridges had to be expected. Therefore it was found possible from the time course of force after the displacement, to estimate for frog muscle: 1. the viscous friction between the filaments; 2. the turnover-rate of the crossbridges. Force-velocity curves, calculated from these data, fitted quite well to A.V. Hill's measurements. Quick shortenings show qualitatively good agreement between frog and rat muscle. The behaviour upon quick stretches, however, suggests differences between both.

GROWTH AND LYSOSOMAL HYDROLASES OF MORRIS HEPATOMAS AT ALTITUDE. C. M. Blatteis, J. P. Filkins, and F. J. Fuste. Depts. of Physiology and Biophysics and Pathology, Univ. of Tenn. Medical Units, Memphis, Tenn. USA.

Buffalo strain rats, with and without transplants of Morris hepatomas 5123C or 7793, were exposed for 8 weeks to sea level or 4,500 meters simulated altitude. Tumor size was measured weekly; and, at sacrifice, final tumor mass, and representative hepatoma, liver and serum acid hydrolases were determined. Hepatomas 5123C of the altitude hosts showed a depressed growth rate, and weighed 50% less at termination, when compared to those of hosts maintained at sea level. These hepatomas at altitude also exhibited significantly decreased β -glucuronidase (BG) and cathepsin D (CD), but unaltered acid phosphatase (AP) and ribonuclease (RN), activities. At sea level host livers contained markedly elevated lysosomal hydrolase activities, while at altitude they showed only slight increases. The activities in livers of non-tumorous rats were not affected by altitude, except that of CD which increased. Host serum AP and BG activities were increased in both environments. Both the morphometric and enzymatic responses in rats bearing hepatomas 7793 were similar in pattern, although more variable in magnitude. The present results would seem to suggest, therefore, that the progression of these rat hepatomas may be retarded by exposure of the hosts to altitude, and that this effect involved alterations in the activities of lysosomal enzymes in both hepatomas and host livers. (Supported in part by A. C. S. Institutional Cancer Research Grant No. IN 85C.)

191 HETEROGENEOUS NATURE OF THE CALCIUM-SENSITIVE BIOLUMINESCENT PROTEIN AEQUORIN.
J. R. Blinks. Department of Pharmacology, Mayo Graduate School of Medicine, Rochester, Minnesota 55901, U.S.A.

Aequorin, extracted from the hydromedusan Aequorea forskålea, emits light in the presence of traces of Ca++, and has considerable promise as a calcium indicator for certain types of physiological studies (Shimomura et al., Science 140:1339, 1963). Aequorin purified by repeated alternate steps of gel-filtration on G-50 Sephadex and ion-exchange chromatography on A-50 DEAE Sephadex, can be resolved into three major components by means of analytical polyacrylamide disc gel electrophoresis at pH 9.3. All of these components emit light on exposure to Ca++. Aequorin treated with sodium dodecyl sulfate (method of Weber and Osborn, J. Biol. Chem. 244:4406, 1969) migrates as a single band on gel electrophoresis, indicating that the three components differ primarily with respect to charge, and not molecular size. Isoelectric focusing also reveals the existence of at least three luminescent components, having isoelectric points (0°C) at pH 4.42, 4.55, and 4.70. Efforts to separate these components in quantities sufficient to allow detailed comparisons of their reaction kinetics have so far been unsuccessful, but are continuing. (Supported by USPHS grants HE 12186 and RR05530, and by the American Heart Association; use of the facilities of the Friday Harbor Laboratories, University of Washington, is gratefully acknowledged.)

AN INPUT TO THE LATERAL RETICULAR NUCLEUS FROM COLLATERALS OF THE DORSAL SPINOCEREBELLAR AND CUNEOCEREBELLAR PATHWAYS. J.R. Bloedel, J.E. Burton, and R.S. Gregory. Lab. of Neurophysiology and Dept. of Neurosurgery, Univ. of Minnesota, Minneapolis, Minnesota, USA.

Previously it was shown that stimulation of the dorsal spinocerebellar and cuneocerebellar pathways activates two groups of mossy fibers. One group projects directly from these pathways to the cerebellar cortex, while the other projects to the cerebellum from other sites, one of which was proposed to be the lateral reticular nucleus (LRN). hypothesis was tested by recording the responses of two types of neurons in the LRN to stimulation of the dorsal spinocerebellar tract (DSCT) and the lateral cuneate nucleus (ECN). Generally, a single spike followed by a long-latency burst response was evoked by these stimuli. The characteristics of the latter were shown to be similar to the responses evoked in the cerebellar cortex by the second group of mossy fibers alluded to above. Additional experiments demonstrated that stimulation of Group I fibers in peripheral nerves was sufficient to evoke these responses in preparations in which all but the ipsilateral dorsolateral fasciculus of the spinal cord was sectioned. Collision experiments showed that LRN neurons could be activated by collaterals of fibers in the DSCT. It was concluded that these collaterals are responsible, at least in part, for the activation of a mossy fiber input from the LRN following DSCT stimulation. A similar collateral system was proposed from the cuneocerebellar pathway.

CHARATERIZATION OF VISUAL SYSTEM NETWORK. B.Blum, S.Gitter, V.Godel, A.Dali, and R.Stein.Dept. of Physiol. & Pharmacol. and Vision Electrophysiol. Res. Lab., Tel-Aviv Univ. Med. Sch., Tel-Aviv, Israel.

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In an attempt to define a minimally required network for mammalian visual function microphysiological evidence was sought for connectivities between regions responding to optical stimuli, which fulfill criterion that impulses initiated in neurones at origin propogate directly to regions of termination of connectivity. Enroute to visual cortex(VC), optic tract branches to superior colliculus(SC), prior to synapsing in lateral geniculate nuclei (LGNDSLGNV).SC is like LGND and pulvinar nucleus(PUL) in receiving fibers from VC.It plays a role in visuomotor integration, which in turn is important for visual perception. It will be shown that SC projects homolaterally to PUL and to LGND and bilaterally to center median (CM). It receives projections homolaterally from PUL and bilaterally from LGND. Since spontaneous neuronal discharges have been assumed to result from excitation by neighbouring neurones, a test for the above mentioned network criterion was applied to them and to optically discharged units:antidromic impulses evoked in projection fiber were timed according to the neuronal discharge to collide with orthodromic impulses if such invaded the fiber. It was thus possible to determine when impulses were carried by the projection fibers in consequence of each type of neuronal discharge. The data revealed an intermittent impulse propogation with some PUL and LGND projecting fibers in contrast to higher rates shown by other fibers projecting to these regions or to CM. These rates did not correlate to fiber size and involvement of integration factor is proposed.

THE NATURE OF RECEPTORS FOR AMPHETAMINE IN THE BRAIN STEM R.J. Boakes, P.B. Bradley & J.M. Candy. MRC Neuropharmacology Unit, Birmingham, England.

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Previous studies have shown that d-amphetamine, applied by micro-iontophoresis to single neurones in the brain stem of unanaesthetised decerebrate cats, mimics both excitatory and inhibitory actions of noradrenaline, and only acts on noradrenaline-sensitive neurones. Similar effects have been observed in halothane-anaesthetised rats and pretreatment with reserpine abolished the actions of d-amphetamine in the rat, whilst responses to noradrenaline were still present. The duration and amplitude of excitatory responses to noradrenaline were increased after reserpine. Similar effects were obtained following pretreatment with $\alpha\text{-me-p-tyrosine}$. After systemic administration of l-dopa to $\alpha\text{-me-p-tyrosine-pretreated}$ rats, responses to amphetamine were again observed. These findings support the hypothesis that the action of d-amphetamine in the brain stem is to release endogenous noradrenaline from nerve terminals.

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UPTAKE OF $[^3H]$ OUABAIN AND Na PUMP TURNOVER RATES IN MONOLAYER CULTURES OF GIRALDI HEART CELLS. Lesley Boardman, J.F. Lamb and D. McCall. Physiology Department, University of St. Andrews, Scotland.

New steady-state Na and K levels were produced by 24 hr. treatment with ouabain or $[^3H]$ ouabain. Under these conditions the $[\mathrm{Na}]_1$ rises markedly, there is a fall in the ouabain sensitive fluxes and a rise in the total $[^3H]$ ouabain uptake. In normal cells the ratio of Na/K is near 3:2 as in other cells; in partially blocked cells this changes to nearly 3:1. We have assumed that for each three molecules of Na transported one ATP molecule is split. 3H -ouabain uptake during 30 min. in K-free $[^3H]$ ouabain was taken as a measure of the number of free pump sites both in normal and previously $[^3H]$ ouabain treated cells. Under the latter conditions this gave an additional uptake. Although we have no direct evidence that ouabain does bind specifically to the pump sites this binding is very $[K]_0$ dependent and the $T_{\frac{1}{2}}$ of loss of the ouabain is similar in normal and partially blocked cells (12-18 hr). The calculated pump turnover rate was about 20sec- 1 in all conditions. This evidence supports the view that these cells are capable of increasing their number of pumping sites, and that these extra pumps have normal turnover rates.

196 FACTORS REGULATING THE SYNTHESIS OF PLASMA FIBRINOGEN. V. Bocci and A. Pacini. Inst. of General Physiology, Univ. of Siena, Siena, Italy.

Plasma fibrinogen concentration can be increased-by a number of stimuli such as injuries, acute and chronic inflammatory diseases, cancer and injections of endotoxin, turpentine, adrenaline, free fatty acids and ACTH. However, in normal conditions, an important stimulus may be represented by fibrinogenolytic products and the possible relationship between these products and fibrinogen synthesis has been investigated. After doubling the fibrinogen mass by infusion of homologous fibrinogen, the concentration in the plasma declines rapidly during the next twelve hours and then doubles in about two days, suggesting that the increased mass of split products may have stimulated the synthesis. This kind of feedback control mechanism does not operate after infusion of homologous albumin, α – and α –globulins and bovine fibrinogen. The effect of derivatives of fibrinogen produced by fibrinolysin is currently under study.

197 INFLUENCE OF NERVUS DEPRESSOR STIMULATION ON CREATININE CLEARANCE, URINE AND ELECTROLYTE EXCRETION IN RABBITS WITH REGARD TO VARIATIONS IN SALT INTAKE. J.Bödeker. Inst.of Physiology, Freie Univ. Berlin, Berlin, Germany

Different quantities of sodium chloride were added to the daily diet of two groups of rabbits. (Group A:0,6mEq Na/kg,Group B:43,0mEq Na/kg). Water diuresis was induced by an i.v.0,6%saline solution. The arterial blood pressure was decreased in steps by electrically stimulating a depressor nerve for 5 min. The effect of this decrease on clearance of creatinine, electrolyte and water excretion and the liberation of an antidiuretic activity was investigated. The difference in the response of the two groups was as follows:

1. In both groups a fall in blood pressure due to stimulation of the depressor nerve resulted in an increase in the tubular reabsorption of filtered sodium and a decrease in water excretion independent of whether the clearance of creatinine remained constant or fell. 2. In group A there was a decrease in clearance of creatinine when mean arterial pressure decreased from 100mmHg to 90mmHg, while in group B creatinine clearance remained unchanged. When blood pressure decreased below 90mmHg, creatinine clearance fell in both groups. 3. Stimulation of the depressor nerve producing a fall in arterial pressure below 90mmHg may liberate an antidiuretic substance. While in group B a ratio Uosmol/Posmol of 5 was possible, in group A a corresponding fall in blood pressure produced a Uosmol/Posmol of maximal 2.0.

PROPERTIES OF HUMAN ERYTHROCYTE GHOST POPULATIONS.

H.Bodemann and H.Passow, Max-Planck-Institut fuer Biophysik, Frankfurt (Main), Germany

The properties of reconstituted erythrocyte ghosts depend on the conditions under which osmotic hemolysis and the subsequent reversal of hemolysis, by the addition of salt to the hemolysate, takes place. The amount of alkali ions which can be incorporated during reversal of hemolysis depends on the temperature at which hemolysis takes place and increases with decreasing temperature. The reconstituted ghosts do not form a uniform population. A somewhat variable fraction of the ghosts is permanently leaky, regardless of the temperature at which hemolysis is performed. When hemolysis and reversal take place at 0°C, the remaining fraction slowly recovers impermeability after warming to 37°C. With osmotic hemolysis at 37°C, this fraction recovers impermeability to cations immediately. Hence, only a small portion of the alkali ions added for reversal enters this fraction. When hemolysis takes place at 25°C, all three types of ghosts exist: Leaky ghosts, ghosts which reseal immediately after hemolysis, and ghosts which reseal only after reversal and prolonged incubation at 37°C. - When complexing agents (ATP, EDTA, 2.3-DPG) are present during hemolysis at 25°C, the majority of the ghosts, and at 37°C, all ghosts remain leaky. When present at 0°C, complexing agents penetrate into the cells and become trapped after subsequent incubation at 37°C. This indicates that the complexing agents are capable of rendering the permeability barrier ineffective to cations when present during hemolysis at elevated temperatures but not afterwards. (Supported by the Deutsche Forschungsgemeinschaft, SFB 38)

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ELECTROPHYSIOLOGICAL FEATURES OF THE GASTRIC SMOOTH MUSCLE. K. Boev. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

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By the modified method of the double sucrose gap studies were made on the stomach of cats and rats. The spontaneous as well as the provoked slow potentials from the cat's stomach were found to have a complex configuration and be always accompanied by muscle contractions. The change in the pattern of slow potentials under the effect of polarizing currents, temperature alterations and mediators was invariably accompanied by the change in the pattern of muscle contractions. Unlike the slow potentials from the cat's stomach, the sinosuidal slow potentials from the rat's stomach were not accompanied by contractions. Muscle contraction was observed just at the appearance of the first spike potentials. We suggest that the pattern of slow potentials from the cat's stomach differ from the sinosuidal slow potentials and are similar to the action potentials from the muscles of the heart, ureter and some blood vessels.

THE MOTILITY AND EVACUATION DISTURBANCES IN THE VAGOTOMIZED STOMACH AND THEIR NORMALIZATION BY GANGLIONIC BLOCKING SUBSTANCES.P.G. Bogach and S.D. Groisman. Shevchenko Kiev State Univ., Kiev, USSR.

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The trunkal bivagotomy in dogs evokes the inhibition of stomach evacu-The trunkal bivagotomy in dogs evokes the inhibition of stomach evacuation and following phasic changes in its motility:1) the inhibition phase, 2) the phase of slow rate uninterrupted strong contractions and 3) the motility stabilization phase. During the last phase in one group of dogs the tendency to the stomach motility normalization was observed. In the other group of dogs the steady stomach hypo-motility was registered. The vagotomy doesn't change the stomach plastic tone and intragastric pressure. The stomach evacuation disturbances were caused by weakening of stomach phasic contractions. The ganglionic blocking substances injections to the vagotomized dogs stimulated the appearance of low rate contractions and brought the normalization of the stomach evacuation. This effect didn't depend on the extramural sympathetic nerves and was determined by the distorted senthe extramural sympathetic nerves and was determined by the distorted sensitivity of Auerbach plexus to the ganglionic blocking substances. The ganglionic blocking substances caused the same effect on the stomach motility and evacuation in the vagotomized human beings. The clinical examinations revealed the effectivity of ganglionic blocking substances as the tool for normalization of stomach evacuation in the vagotomized men.

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BIOELECTRICAL ACTIVITY IN DIFFERENT REGIONS OF THE STOMACH AND ITS RELATION TO THE CONTRACTION. P.G. Bogatch, K.T. Milenov, N.A. Kaplunenko. Inst. of Physiology, Sofia, Bulgaria, Inst. of Physiology, Kiev, USSR.

The bioelectrical activity of the fundus, body and antrum of the stomach in rats, mice and guinea pigs was studied in vitro and in vivo by way of macroelectrodes, pressure electrodes, double sucrose gap and micro electrodes. From the muscles of the fundus as well as from single smoothmuscle cells are recorded continuous oscillations of the membrane potential with a frequency of 60 to 70 cpm. Each oscillation could generate a spike (action potential). The action potential triggers the increase in the tone. From the muscles of the body and antrum as well as from the single smooth-muscle cells are recorded biopotentials in the rhythm of the peristalsis (4-6 cpm). The cell membrane potential from these regions fluctuates in the form of sinosuid on which brushes of spikes are superimposed. The membrane potential of the smooth-muscle cells in the gastric regions in rats and mice, at 38°C, is 25 to 52 mv, in the antrum of the guinea pig it is 25 to 55 mv (36 - 1.1). At 35°C the membrane potential was found to have higher values (40 to 70 mv).

202 HEART RATE CHANGES DURING FEAR EXTINCTION IN RATS TREATED WITH PITUITARY PEPTIDES OR CORTICOSTEROIDS. B. Bohus, D. de Wied, K. Lissák. Inst. of Physiology, Univ. Med. Sch., Pécs, Hungary and Rudolf Magnus Inst. for Pharmacology, Univ. of Utrecht, The Netherlands.

We have previously shown that pituitary peptides like ACTH or vasopressin delay whereas adrenocortical hormones enhance the extinction of conditioned avoidance responses of the rat. Present experiments showed that an autonomic response during conditioned fear extinction is also influenced by these hormones but in the opposite directions. Male rats were conditioned by pairing the conditional stimulus of a tone with the unconditional stimulus of an unescapable electric foot shock (signalled emotional conditioning) or by unescapable shock at fixed intervals without a warning stimulus (nonsignalled conditioning). Heart rate of free-moving rats was recorded by electrocardiography. A delay of extinction of heart rate change was observed in the signalled situation in rats treated with 1.0 mg cortisone daily throughout 10 days of extinction. In contrast, ACTH administration (20 μg) facilitated extinction of the cardiac response. Extinction of the autonomic response in the non-signalled situation was not affected by the hormones. The effect of ACTH-like peptides and vasopressin as well as the relation between somatomotor and autonomic changes in the hormone-treated rats will be discussed in terms of emotionality and/or fear level.

MACRO- AND MICROELECTRODES STUDIES OF MOTOR CORTEX VESTIBULAR RESPONSES. N. Boisacq-Schepens and M. Hanus. Laboratory of Neurophysiology, University of Louvain, Belgium.

Electrical stimulation of the ampullar nerve from the horizontal semi-circular canal was used to demonstrate vestibular input to the motor cortex of chloralosed cats. Macroelectrode recordings of the cortical surface responses show two kinds of evoked potentials: the ones, restricted to the postcruciate dimple, are evoked after a brief latency (5 to 6 msec); the others, more variable and widely dispersed, have a longer latency (10 to 15 msec). These facts as well as results from occlusion experiments (conditioning somatic stimulation preceding the ampullar test shock) suggest that two differents populations of neurons are involved in these responses. Microelectrodextracellular studies of somatic and vestibular inputs and of pyramidal output (tested by antidromic invasion from bulbar pyramid) of motor cortex neurons show two prominent facts: the vestibular afferents reaching some 40 % of the neuronal pool studied, seem to be selectively distributed to the widely convergent somatic neurons; some of these vestibular neurons are pyramidal-tract neurons. This macro- and microphysiological approach of the motor cortex shows the importance of vestibular input to this cortical area, particularly in relation to other sensory inputs as well as to pyramidal output.

ROLE OF A MEMBRANE CA FRACTION IN E-C COUPLING IN SKELETAL MUSCLE. C. Bonciocat. Inst. of Physiology, Bucharest, Romania.

Lauryl-sulphate (LS)(2-5xlo⁻⁵ M) potentiates K contractures in frog toe muscle in Tris solution.Unexpectedly, EDTA determines a contracture in normal tris solution (threshold about 5 mM).LS potentiation of K contracture is associated to a potentiation of EDTA response with similar kinetics (half-time 3 min).The rather minor depolarization during potentiated EDTA contracture which is abolished after osmotic shock with glycerol suggest a T system mechanism.LS does not alter caffeine contracture. Caffeine in potentiating concentrations has no significant effect on EDTA response. These facts indicate that LS potentiation of K contracture has like EDTA contracture a surface mechanism.NO₂ considered to act on surface structures has no effect on EDTA response. LS addition increases NO₂ potentiation and develops its own EDTA response. Two mechanisms can ope 2 rate in membrane dependent E-C coupling alterations caused by a shift in mechanical threshold: LS type, in which a fraction of membrane Ca (probably T system) is directly involved; NO₂ type, which by altering local responses to depolarization can indirectly involve the same Ca fraction. This membrane Ca fraction may also play a role in normal E-C coupling.

EFFECTS OF AN 4 TO 8 HOUR-IMMERSION ON BLOOD COMPOSITION, BLOOD VOLUME AND URINE EXCRETION IN TRAINED AND UNTRAINED PERSONS. D. BÖNING. Physiol. Inst. Deutsche Sporthochschule, 5 Köln 41, Germany (Fed. Rep.).

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The aim of the experiments was to explore 1) influences of immersion on blood and urine in short intervals, 2) possible differences between trained and untrained subjects during immersion. Urine excretion was stimulated in a larger amount and more rapidly in the untrained subjects. Electrolyte excretion increased to a similar amount in both groups. Plasma electrolyte concentrations showed the following changes: K a reversible increase in both groups, Na parallel fluctuations during the first 4 hours in both groups, P: a steady increase in both groups; osmotic pressure was higher in the untrained group at the end of immersion. In the red cells the sodium and chloride concentrations decreased slightly. Plasma volume was diminished at the end of the immersion by 5-10 %. There was a tendency to a smaller decrease in the trained subjects. The volume regulation by atrium distension and following change of adiuretin secretion seems to be less sensitive in trained than in untrained subjects.

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REPEATED HEART BEATS OF ATRIAL ORIGIN AFTER AN EARLY PREMATURE BEAT. F.I.M. Bonke, L.N. Bouman, F.J. Schopman. Dept. of Physiology, Univ. of Amsterdam, The Netherlands.

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During a previous study concerning the effect of early premature beats on heart rhythm and pacemaker activity it was found that a stimulus applied very early in diastole could be followed by a rapid series of discharges that did not seem to be generated by the sino-atrial pacemaker. In an attempt to elucidate this phenomenon we did experiments in isolated rabbit left atria that were quiescent prior to stimulation. Transmembrane action potentials and the surface electrogram were recorded while the preparation was driven with a control interval of 350 msec. Subsequent to 20 stimuli a test stimulus of double strength was given after a delay of 50-80 msec; than the control stimulus was arrested for 1 or 2 sec.

The test stimulus was frequently followed by a train of several, sometimes even more than 30, rapid discharges; the action potentials during such a period had a small amplitude, a short duration and started at a relative low membrane potential. The same phenomena were observed in spontaneously beating right atria after a premature beat that was elicited very early in diastole. We assume at present that by a very early stimulus in the atrium a series of repeatedly re-entering beats can be induced.

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ABSOLUTE RATES AND INTRAFENAL DISTRIBUTION OF SINCLE GLOMERULAR FILTRATION: THEIR RELATION TO THE JUXTAGLOMERULAR INDEX (JGI) IN DIFFERENT TYPES OF EXPERIMENTAL ARTERIAL HYPERTENSION. J-P.Bonvalet, G.Berjal, L.Petit, P.Pencsath, C.de Rouffignac. Dept. of Riol., CEN-Saclay, 91, and U2 INSERM, Hôp. L.Bernard, 94, Brévannes, France.

Single glomerular filtration rate (sqfr) of superficial (S) and juxtamedullary (JM) nephrons was measured by the 14-C ferrocyanide infusion technique in four groups of hypertensive rats (HR), and the JGI of the experimental kidneys was also determined. "Acute" FR:1./90 min of aortic constriction between the two renal arteries (n=6,blood pressure(FP)=163+3 S.E.M. mmHg);2./carotid clamping with or without cervical vacotomy (n=4,FP=146+5 mmHg).
"Chronic" HR:3./4 weeks of Coldblatt hypertension (n=5,FP=187+10 mmHg);4./3 weeks of sodium rich diet plus acute iv. salt loading(n=5,FP=150+5 mmHg). In 10 control rats results were: sqfrs=32.7+1.4;sqfrJM=41.1+1.9 nl/min;JGI=36+9,with predominant granularity in S nephrons. In "acute" HR sqfr's were not different from control values:1./S=30.3+3.0;JM=41.0+4.5,2./S=30.9+3.3;JM=38.9+4.8 nl/min and JGI was slightly reduced with S predominance maintained: 1./22+2,2./31+8.0ppositely,sqfr's were markedly augmented in "chronic" HR:3./S=73.0+8.4; JM=74.7+8.2, 4./S=52.4+3.2;JM=52.7+4.3 nl/min,while JGI was equal to zero,Thus,sqfr's increased only in groups where JGI was suppressed.Moreover, in these groups no more difference between S and JM sqfr's was seen(sqfrs/sqfrJM=0.978+0.034 and 1.024+0.072,respectively), contrasting with control and "acute" groups (0.797+0.020, 0.746+0.020 and 0.810+0.050, respectively). In conclusion, an inverse relationship between filtration rate and granularity of individual nephrons can be suggested.

A COMPARISON OF THE ACTIONS OF NOREPINEPHRINE AND CYCLIC AMP ON ACTIVE POTASSIUM TRANSPORT. P. G. Borasio and M. Vassalle. Department of Physiology, State University of New York, Downstate Medical Center, Brooklyn, N. Y., U. S. A.

The aim of this investigation was to determine whether norepinephrine-induced increase in potassium uptake can be mimicked by dibutyryl adenosine 3':5'-cyclic monophosphoric acid (cyclic AMP). Canine ventricular Purkinje fibers were mounted in a tissue bath near a beta detector and loaded to equilibrium with $^{42}\mathrm{K}$. Tissue radioactivity and transmembrane potentials were measured at the same time. With the fibers electrically driven, 3 x 10^6 M norepinephrine caused an increase in K uptake which was reduced or abolished in the presence of 2-deoxy-D-glucose, strophanthidin, tetrodotoxin, propanolol and in the absence of Na $^+$ or Mg $^+$. Cyclic AMP (10 $^-$ M) similarly provoked an increase in K uptake: this increase was blocked by propanolol and was reduced in Mg $^+$ - free solution. Low doses of either norepinephrine (3 x 10 $^-$ M) or cyclic AMP (10 $^-$ M) caused a diminution in K uptake; alpha blockade abolished this effect of cyclic AMP. It is concluded that cyclic AMP can mimic the actions of norepinephrine on active K uptake, possibly through some form of adrenergic activation.

Supported by a grant from New York Heart Association.

CARDIAC ACCELERATION INSTANTANEOUSLY FOLLOWING THE ONSET OF VOLUNTARY MUSCLE CONTRACTION. C. Borst, A.P. Hollander and L.N. Bouman. Dept. of Physiology, Univ. of Amsterdam, The Netherlands.

Changes in heart rate following a strong isometric contraction of less than 1 sec duration were studied in 14 human subjects. In each experiment 30 contractions were performed. The results show: (1) both plantar flexion of the foot (10 experiments) and contraction of the masticatory muscles (9 experiments) were followed by cardiac acceleration starting 450-650 msec after the onset of the contraction; (2) when a contraction began early in an R-R interval that same interval was shortened; (3) the maximal average decrease of the cardiac interval ranged between 4-19% after plantar flexion, between 4-11% after contraction of the masticatory muscles; (4) the maximal response was near the lower value when the heart rate exceeded 80/min (R-R interval < 750 msec); (5) there was no difference in response between plantar flexion with one foot and two feet (10 experiments). We conclude that, regardless of the mass of muscles used, any strong contraction is instantaneously followed by cardiac acceleration as a result of vagal inhibition.

BLOOD NEFA AND BLOOD GLUCOSE IN FED OR FASTED SHEEP. J. Bost and R. Boivin Ecole Nationale Vétérinaire de Lyon, FRANCE.

Blood samples were automatically and permanently drawn from the jugular vein of conscious sheep restrained in their pens. Small doses of heparin were constantly delivered at the tip of the jugular catheter. Feeding behaviour and rumination were simultaneously recorded. Determinations have been made on more than 1000 samples, each one collected every two hours. In fed sheep, blood NEFA vary from 200 to 550 pequ./1. Daily variations are observed with one or two peaks. Most often, there is a peak in the early morning but no constant pattern can be established in any animal. Blood glucose usually ranges from 450 to 650 mg/l and varies randomly (extreme values: 300 mg and 1000 mg/l). When fasting, the NEFA level rises during the first 3 or 6 days, reaching 1050 to 1075 requ./l. In the same time, there is no decrease of blood glucose. Irregular NEFA fluctuations are still to be seen during fasting. Neither NEFA nor glucose variations can be correlated with feeding or rumination activity.

HISTAMINE-MEDIATED AIRWAY RESPONSES IN MAN. A. Bouhuys, J.S. Douglas and A.R. Guyatt.

John B. Pierce Fndn., Yale Univ. Sch. Med., New Haven, Conn. 06519, U.S.A.

Cotton and hemp fiber dust induce acute bronchoconstriction, probably via release of histamine in the lungs, in about 70% of healthy people; long-term exposure in textile workers leads to chronic obstructive lung disease. Physiological tests can distinguish "reactors" and "non-reactors" to these dusts. The present study, performed in Callosa de Segura, Spain, concerns mechanisms that may underlie the individual differences in response to hemp dust and to histamine. We used partial (PEFV) and full maximum expiratory flow-volume (MEFV) curves (J.Clin.Invest.48:1159,1969) to quantitatively assess airway constriction induced by histamine aerosols and by hemp dust in 3 healthy volunteers and 8 hemp workers. Histamine (2 min. exposure) induced dose-related decreases of flow rates on PEFV and MEFV curves. Hemp dust exposure (1-6 hrs.) induced similar changes in "reactors". Severe responses to both agents led to dyspnea and chest tightness; slight responses did not cause symptoms and showed first as decreased flow rates on PEFV curves. Atropine (1 mg s.c.) inhibited responses to dust and to histamine; propranolol (40 mg orally) potentiated both. These drugs interact similarly with histamine in guinea pigs (Clin. Res. 16:560, 1968). The variability of airway responses to bronchoconstrictor agents may at least in part depend on differences in the balance between vagal and sympathetic impulses that reach airway smooth muscle cells. Interaction between inhaled agents and endogenous neural and/or humoral stimuli, at the cellular level, may help to determine airway responses to dusts and air pollutants in man. Supported by USPHS grants.

INSTANTANEOUS FORCE-VELOCITY RELATION IN HUMAN MUSCLE. S. Bouisset and E. Pertuzon. Lab. of Gen. Physiology, University of Sciences, Lille, FRANCE.

In force-velocity curves concerning isolated muscle, <u>isotonic</u> forces are plotted against corresponding maximal velocities of muscle shortening. These relations were established under some precise conditions which are different from those of a natural movement, for example voluntary human movements performed against <u>inertias</u>.

Therefore, as far as that type of movements is concerned, it is necessary to study the relation between instantaneous values of force and velocity of muscle shortening. During maximal elbow flexions, the calculation of instantaneous values of these two variables was carried out by means of an on-line analog computer.

Experimental results show an hyperbolic relation between force and velocity. This relation is independent from inertia and is not different from the ones previously set up by FENN and MARSH (1935) or by HILL (1938).

DISTRIBUTION OF DOPAMINE AND METABOLITES IN CAT TISSUES AFTER INTRAVENOUS INFUSION.

D. J. Boullin & R. A. O'Brien. Lab. Preclin. Pharmacol., NIMH, Washington, D.C. 20032,USA.

We have mimicked plasma dopamine concentrations noted in L-DOPA treated parkinsonian patients by i.v. infusion of 0.2 \(\mu\text{mon}\) 1/\text{Mon} 1/\text{Gopamine} (rate: 280 \text{ nmol/min for about 2 min.)} into cats. One min. after the end of infusion, 84-90% of the radioactivity had left the circulation. About 55% was recovered in 11 tissues from 9 organs. 29.8% was dopamine metabolites and 24.2% was unmetabolized amine. Also, 2.3±0.3% (mis.E.) dopamine was in the blood platelets and 3.0±0.9% (mis.E.) dopamine in the urine. The tissues could be grouped according to concentrations of dopamine & metabolites: 1) Low dopamine (<700 pmols/g), low metabolites (<300 pmols/g); adrenal glands, auricle, diaphragm, pyloric and fundic stomach, intestine. 2) High dopamine (>700 pmols/g), low metabolites; platelets, ventricle, spleen.

3) High dopamine and metabolites (>300 pmols/g); kidney. 4) Low dopamine, high metabolites; lung and liver. Tissue to plasma dopamine concentration ratios (CT/Cp) were highest in platelets (207), kidney (16) and spleen (8); other tissues were in the range 1.5-5.8. In most tissues metabolites were acid, alcohol, or aldehyde derivatives; in liver and lung there were small amounts of 3-methoxydopamine, but no detectable noradrenaline. The major organs removing dopamine from the circulation were kidney (excretion), liver & lung (metabolism), and platelets, ventricle, kidney and spleen (accumulation against a concentration gradient). The rapid inactivation of peripheral circulating dopamine by several mechanisms would help explain the high doses of L-DOPA required to raise cerebral dopamine in the treatment of Parkinson's disease.

214 EVIDENCE FOR INTERCELLULAR PASSIVE ION PERMEATION ACROSS THE PROXIMAL KIDNEY TUBULE.

Emile L. Boulpaep and John F. Seely. Dept. Physiol. Yale Univ. New Haven, Conn. U.S.A.

The view that passive ion movement occurs through the tight junctions of proximal tubular epithelium is supported by: 1) Interaction phenomena i.e. potential changes at either the luminal membrane (LU) or peritubular membrane (PT) evoked by changes in ion composition at the contralateral cell membrane are explained by an extracellular shunt path in parallel with the PT and LU in series. 2) The very low value of the specific transepithelial resistance (R) in both Necturus (70 ohm.cm²) and dog (5.6 ohm.cm²) and the demonstration in Necturus of a PT or LU resistance two orders of magnitude larger, indicate that R reflects an intercellular path. 3) Transepithelial current-voltage relationships measured with short pulses are linear, while the PT in Necturus shows anomalous rectification. 4) Relative ionic permeabilities across dog proximal epithelium show that anions are restricted relative to cations, but relative to one another permeate as expected from their behaviour in free solution. The transepithelial selectivity pattern i.e. the range and ranking of the ionic permeability coefficients differs strikingly from the selectivity pattern of PT or LU. 5) Transepithelial permeation can be considered as occurring across a single membrane as evidenced by the good agreement between two experimental approaches for the determination of a transepithelial ion transference number: one from salt gradients treating bhe epithelium as a single barrier, the other independent of such assumption using determinations of R_m.

FREQUENCY DEPENDENCE OF SODIUM GRADIENT IN ATRIAL MUSCLE. L.N. Bouman, F.J. Schopman, F.I.M. Bonke. Dept. of Physiology, Univ. of Amsterdam, The Netherlands.

In the isolated crista terminalis of rabbit right atria transmembrane action potentials and their first time derivative were recorded while extracellular sodium concentration, [Na]o, was varied in steps between 60% and 125% of control (156 mM). Osmotic differences were balanced by adding mannitol. The preparation was driven with frequencies ranging between 3 and 6 c.p.s. The main results are: 1. In the tested range of [Na]o the maximal dV/dt shows an exponential decay with decreasing [Na]o, from 115% to 60% of the value at control [Na]o. Max. dV/dt was reached at a membrane voltage of about -35 mV, inside negative, regardless of [Na]o and frequency. 2. From phase plane trajectories maximal ionic current at normal [Na]o was calculated to be about 0.4 mA/cm², at a membrane voltage of about -20 mV. To varying [Na]o current was related in the same way as dV/dt max. 3. Also the amplitude of the a.p. decreases exponentially with [Na]o from 105% to 90%. 4. If frequency is changed from 3 to 6 c.p.s. there is a linear decay of both dV/dt max. (9%) and amplitude (3%). The assumption is made that these changes are entirely caused by an increase of internal [Na]. From the results mentioned above the amount of sodium accumulation was estimated to be about 5% when heart rate increases with 1 c.p.s.

216 CELLULAR OSMOLARITY AND TRANSEPITHELIAL WATER PERMEABILITY IN FROG URINARY BLADDER. J. Bourguet, M.Parisi and P.Ripoche, Dept de Biol., C.E.N., Saclay, France.

The hydrosmotic action of hypertonic media has been attributed to biochemical modifications also involved in the action of antidiuretic hormone. It was of interest to establish the existence of an opposite reaction to cellular hypotonicity, a condition normally associated to high transepithelial water net fluxes. Bladders were thus exposed to oxytocin in absence of osmotic pressure difference, so that no increase of the water net flux could take place. After 15 minutes, the driving force was rapidly established, by diluting the mucosal solution. In these conditions an overshoot is observed in the evolution of the water net flux. The flux reaches a maximum in 2 to 3 minutes, but after, it progressively decreases to a considerably lower equilibrium value, indicating that the establishment of a water flux, presumably via the resulting hypotonicity, is followed by a reduction of the osmotic permeability of the preparation. It thus appe It thus appears that both an increase or a decrease of osmolarity can modify the water permeability and the water net flux in a manner which will tend to correct the initial alteration of osmolarity. Furthermore, the mechanisms involved in this regulation appear to be narrowly linked to the hormonal mechanism of action.

PATHWAY OF RESPIRED GAS IN THE AIR SACS-LUNG APPARATUS OF DOMESTIC FOWL. P. Bouverot and P. Dejours. Laboratoire de Physiologie Respiratoire, CNRS, Strasbourg, France.

The pathway of respired gas in birds has been explained in two ways. According to Zeuthen, all parts of the air sacs-lung apparatus have a bidirectional tidal ventilation. In the theory of Bethe-Hazelhoff, the gas flow of the parenchymal parabronchi is unidirectional from caudad to rostrad, during inspiration as well as expiration.

CO2 was used as a tracer to follow the sequence of invasion of the air sacs-lung apparatus in anesthetized, upright fowl breathing air. Cycle-to-cycle changes in total gas pressure and $P_{\rm CO2}$ in abdominal air sacs (AbAS) and interclavicular air sac (IcAS), and in $P_{\rm CO2}$ of tracheal gas, were simultaneously recorded. Changes of total pressure in AbAS and IcAS were in phase. When the animal was switched suddenly to a high CO2 mixture the increase of $P_{\rm CO2}$ in tracheal gas and AbAS was almost simultaneous, while that of IcAS lagged and was damped. Injection of CO2 into AbAS was followed by a damped increase of IcAS $P_{\rm CO2}$. Injection of CO2 into IcAS did not affect AbAS $P_{\rm CO2}$ or arterial $P_{\rm CO2}$. These findings support the Bethe-Hazelhoff concept of a unidirectional gas pathway in birds.

SODIUM TRANSPORT AND OXYGEN UTILIZATION IN THE ISOLATED PERFUSED RAT KIDNEY. R.H.Bowman.Veterans Admin.Hosp., Upstate Med.Ctr., Syracuse, N.Y.13210, U.S.A.

Considerable evidence indicates a causal relationship between sodium transport and oxygen utilization in the kidney. Renal oxygen uptake has been shown also to be positively related to blood flow, and evidence for a constant Na/O₂ ratio has been derived, for the most part, from experiments in which the filtered sodium load and renal blood flow have varied together. To study this problem we have conducted experiments with the isolated perfused kidney in which changes in sodium load can be dissociated from rate of blood flow. Perfusate consisted of bicarbonate buffer containing bovine serum albumin and was equilibrated with 95% O2/5% CO2. Oxygen tension in the influent and effluent was continuously monitored with polarographic electrodes. Sodium load was altered by changing perfusate oncotic pressure, perfusion pressure, or perfusate sodium concentration. Without exogenous substrate, oxygen uptake ranged between 2 and 10 µmoles/g/min, and showed little relationship to net sodium transport. High oncotic pressure (10% albumin) reduced GFR to nearly zero but did not appreciably alter perfusion flow rate or oxygen uptake. Acute addition of substrate (pyruvate) or acute increase in net sodium transport caused oxygen uptake to increase. The data suggest that functions of the kidney aside from sodium transport contribute significantly to oxygen utilization by this organ.

ON THE ELECTROMYSTOLOGY OF CYTOPLASHATIC MEMICANES: ABOUT THE INFIDENCE OF POTASSIUM AND CHECKIDE IONS ON THE MEMICANE POTENTIAL OF MYELINATED MEMVE FIBRES. M. Bradl. Inst. of Physiology, Univ. of Jena, DDR.

By the principle of the sucrose gup method the influence of potassium and chloride ions on the resting potential of myelinated nerve fibres has been studied. The fibres were used both in fresh state and after equilibration in different electrolyte solutions. On fresh fibres the measurements have shown the existence of two potential components, which are sensible the one to potassium and the other to chloride ions and which contribute additively and independent upon one other to the total nembrane potential. The effect of the ions may be partially modificated by equilibration. In order to explain these results, the plasmolerm has been treated as a microheterogenic system with respect to the ultrastructure and physical chemistry of the cytoplasmatic membrane. In this view, the resting potential seems to be an expression of phase boundary processes within this system, so that the potassium potential will arise at another phase boundary of the membrane than the chloride potential. At equilibration of the nerve filtres there may occure a change in configuration of the membrane lipids.

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CONTRIBUTION OF AV-SHUNTS TO THE CIRCULATION IN SKIN AND MUSCLE.

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In a skin and a muscle area of the hindleg of the anaesthetized dog, the contribution of non-exchanging vessels - av-shunts - to the circulation is studied, using a double isotope dilution technique. A small amount of a mixture of a non-exchanging and an easily exchanging indicator (131 I-albumine and 24 NaCl or 42 KCl respectively) is injected rapidly into a peripheral artery. Pumping the blood from a corresponding vein through an extracorporal flow loop enables the continious measurement of the outflow concentration as a function of time for both indicators simultaneously. The recovery of exchanging indicator results not only from the av-shunts but also from the capillaries due to an incomplete exchange. The dependency of the capillary exchange upon the mean transit time has been used to made a distinction between both contributions. The effect of tissue tracer wash-out has been taken into account. In that way the fractional blood flow rate and blood volume in the capillaries and the av-shunts can be found. In the skin area the results point to an appreciable av-shunt contribution (60-707); in the muscle area an av-shunt fraction of about 30% is found. Changes in the flow and volume distribution has been demonstrated in reaction upon some physiological and pharmacological stimuli.

CALORIGENIC RESPONSES AND SUBCELLULAR MYOCARDIAL IONIC SHIFTS IN ISOPROTERENOL-TREATED RATS
P.O.Bramante and E.L.Nirdlinger, Dept. of Physiology, University of Illinois College of Medicine, Chicago, Illinois, U.S.A.

The pathogenesis of cardiac necrosis induced in the rat by isoproterenol is still unclear. The hypothesis of a relative ischemia produced by increased myocardial 0_2 demand, does not adequately explain the role of cardiac ionic changes as temporally related with the acute calorigenic effects of the drug. Changes of 0_2 consumption (\mathring{V}_{0_2}) were measured with an apparatus (J.Appl.Physiol.14:1063,1959) and method (ibid. 16:982,1961;24:11,1968; The Physiologist, 12:182,1969) which permit continuous quantitation of the metabolic effects of experimental procedures in the intact, awake rat, unbiased by the calorigenic influence of movement (SMA, spontaneous muscular activity). Isoproterenol (40 mg/kg, s.c.) elicited rapid increase of the "net" \mathring{V}_{0_2} (MCMR, minimal calculated metabolic rate) with peaks of 150% after one hour and slow return to normal. During this early calorigenic phase, a significant cardiac mitochondrial Mg decrease with concomitant Ca increase was detected. Subsequently (3-48 hrs after inj.), the mitochondrial Ca rose again, with a 5-fold increase at 24 hrs and return to control levels by 48 hrs. During this delayed phase, a decreased caloric efficiency of the cardiopathic rats was revealed by disproportionate elevation of MCMR during episodes of SMA. However, the resting \mathring{V}_{0_2} (MOMR, minimal observed metabolic rate) was normal. While these metabolic changes could provide a diagnostic tool for the evaluation of experimentally produced cardiopathies, the biphasic mitochondrial accumulation of Ca suggests impaired ability of the cardiac cells to synthesize high-energy compounds.

222 STATIC AND DYNAMIC FRICTION BETWEEN PLEURAL MEMBRANES. G. Brandi. Ist. Fisiologia Umana dell'Università, Modena, Italia.

The force (Fmin.) sufficient to overcome the pleural friction is given by the product of the coefficient of static friction $(\mu_{\rm S})$, the surface area (A) and the pressure (Pad.) which keeps the pleuras together. (Fmin. = $\mu_{\rm S}$. A . Pad.). Pad. is the difference between recoil pressure (Ppl.) and liquid pressure (Pliq.) which are fairly well known. Thus, with experimental values of $\mu_{\rm S}$ and assumed values of A it is possible to calculated Fmin. To this end, $\mu_{\rm S}$ was determined in pleural specimens of rabbits, lubricated with saline: $\mu_{\rm S}$ was found to vary from 0.08 to 0.12 according to the type of preparation. Measurements of the coefficient of dynamic friction ($\mu_{\rm K}$) have shown that $\mu_{\rm K}$ is practically independent from the velocity of sliding and is invariably lower (from 10% to 30%) than $\mu_{\rm S}$. Both $\mu_{\rm S}$ and $\mu_{\rm K}$ appear to decrease with increasing Pad. With extreme values of $\mu_{\rm S}$ and $\mu_{\rm K}$, and assuming A = 1000 cm² and Pad. = 5 cmH₂O, the transdiaphragmatic pressure necessary to produce longitudinal sliding of the lung is from 1 to 1.8 cmH₂O, which is much higher than previous estimates. The values of $\mu_{\rm S}$, as well as considerations of geometry, suggest that pleural friction can be a critical factor for the response of the lungs to accelerations.

MICROCIRCULATION IN CAT SKELETAL MUSCLE AT LOW FLOW STATES.Brånemark,P-I., Eriksson,E.and B.Lisander.Depts of Anatomy and Physiology,University of Göteborg,Sweden.

With the tenuissimus muscle exposed for vital microscopy, the effects on macro- and microcirculation of aortic compression and hemorrhagic shock were studied. In the first case, arterial pressure in the hindlimb was kept at 50mm Hg for two hours, and in the latter, the animal was bled to an arterial pressure of 50mm Hg, which was maintained for two hours. The animal was then observed during four hours. - During aortic compression, the linear flow rates in the arterioles decreased, and they became fully dilated. There was a slight decrease in linear flow rates in capillaries and venules, and a small decrease in the internal diameters of the venules. No aggregation or formation of thrombi were seen. - When the cat was bled to the same pressure level, the same phenomena occurred, and in addition, aggregation of platelets, and changes in the intercorpuscular relation between erythrocytes and leucocytes. The aggregates remained during the whole observation period, irreversibly plugging a lot of small arterioles, capillaries and venules. In those capillaries open, the linear flow rates were even higher than in the pre-shock state e.g. a functional shunting was established. No distinctly delineated precapillary sphincter activity was observed.

THE INFLUENCE OF ANTIDIURETIC HORMONE (ADH) ON THE REGULATION OF THE ARTERIAL PRESSURE. A.Brattström. Inst.of Physiology, Med.Academy Magdeburg, Germ.Dem.Rep.

The excitation of the pressoreceptors of the carotid sinus is reflected in the antidiuretic activity in the serum. Hemorrhage, anesthesia and stress of surgical procedures also change the ADH level. However the influence of ADH on the regulation of blood pressure is not well known. In 28 dogs anesthetized with morphine urethane the influence of ADH in the "Blutdruckcharakteristik" (E.Koch, input-output relation of the carotid-sinus reflex) was investigated. The vagoaortic nerves were cut. Strong doses of ADH were applied as follows. 1.locally. The ADH was added to the Ringer solution which was introduced into the carotid sinus. 2.intravenously by continu ous infusion. 3.centrally, by exchange of 1 ml of liquor with 1 ml of synthetic liquor (0,5-2 µU ADH/kg body weight). In some cases, in which the vagi were intact while the aortic nerves were cut the change of heart rate with increased pressure in the carotic sinus was recorded. The results of these experiments indicate an appreciable reduction of inhibition of the central sympathetic activity by ADH.

ENERGY DEPENDENT REDOX CHANGES OF RESPIRATORY CHAIN AND GLYCOLYTIC COMPONENTS DURING SYNAPTIC TRANSMISSION. B.Brauser, M.Dolivo and Th.Bücher. Inst.of Physiol.Chemistry, Munich, Germany and Inst.of Physiology Lausanne, Switzerland.

To study the coupling of energy demand and redox pattern of the respiratory chain within intact nervous tissue, sensitive spectrophotometric techniques were adapted to the isolated sympathetic rat ganglion during transitions from the resting to the active state. In the resting ganglion the redox degree of cytochromes indicates a highly controlled state: cyt[a+a_z]=<0,03; cyt c=0,15 and cyt b=0,5. Immediately after start of synaptic activity this pattern flattens to the oxidized state due to increased flow of electrons. Concomitant with the oxidation of mitochondrial pyridine nucleotides a slower reduction of cytosolic NADH occurs when glucose is substrate, indicating increased glycolytic flux. Thus a differentiation of cytosolic and mitochondrial energy sources is obtained. Pyruvate serves as important hydrogen donor for the mitochondrial NAD system; half saturation occurs at 1,8mM.

For quantitative evaluation of cytosolic NADH a linear relationship between the reciprocals of [L/P-1] and NADH fluorescence was obtained, L/P being the ratio of lactate and pyruvate in the perfusion fluid.

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THE HYPOTHALAMIC BASIS FOR OBESITY IN GENETICALLY OBESE RATS. 226 and D.A. York. Depts. Med., UCLA School of Med., Los Angeles, California; and Harbor General Hospital, Torrance, California.

The 'fatty' rat is one of several species in which obesity is inherited

as a Mendelian recessive trait. The present studies have explored the possibility that the primary defect producing obesity is in the hypothalamus. The genetically obese rat ate more food (18 vs. 13 g/d) and drank more water (28 ml/d vs. 22 ml/d) than lean rats. Polydipsia persisted even when rats were pair-fed to produce similar solute intake or when they were treated with vasopressin. Thyroid activity was also reduced in the obese animals. Uptake and turnover of radioactive iodine was depressed (uptake 12% vs. 22%; turnover $[t_{1/2}]$ 1 d vs. 3 d). When exposed to cold (3 C), body temperature of opese rats dropped and the turnover of thyroid iodine showed less increase than in the lean animals. Estrus cycles are infrequent in the obese females and their ovaries and uteri are atrophic. Although the pituitaries of obese rats were smaller than those of lean rats, the concentration of TSH (4.8 vs. 4.4 mU/mg) and growth hormone (assessed by acrylamide gel electrophoresis) did not differ. In conclusion, these studies suggest that the nypothalamus may be the site of the defect producing obesity in the genetically fat rat, 'fatty'.

BIVENTRICULAR CARDIAC ASSISTANCE DURING BARBITURATE INDUCED CIRCULATORY ARREST. 227 G. A. Brecher, W. H. Massion, P. E. Downs and N. M. Powell. Dept. of Physiology and Biophysics, Univ. of Okla. Med. Ctr., Oklahoma City, Okla., U.S.A.

Animal experiments were designed to determine if toxic substances, which ordinarily cause irreversible cardiac arrest or failure, can be removed from the body by maintaining the circulation through cardiac massage. Cardiac arrest was induced by a bolus injection of 46 mg/kg thiopental in open-chest dogs. The circulation was then supported with a biventricular assister, either the "Anstadt-cup" or "Brecher-beaker" (Anstadt, G. L. et al. Trans. Amer. Soc. Artif. Int. Organs 12:72, 1966 and Brecher, G. A. et al. Clin. Res. 18: 21, 1970). Each of these devices has a semirigid shell, which is slipped over both ventricles, and a pliable inner lining. The space between shell and lining is alternately inflated with positive and deflated with negative pressures. Thereby the ventricles can be massaged at optimal frequency, force of compression (systole) and dilation (diastole) and at a variable systole: diastole time ratio. Tissue perfusion was maintained at near normal arterial blood pressures until the barbiturate level had decreased sufficiently for spontaneous recovery of normal heart function, followed by survival of the animal. This method has distinct advantages over assistance through extracorporeal techniques. It permits a shorter delay to apply the device, prevents trauma to blood and avoids complications from heparinization and hemodilution. It is concluded that this new approach may be of benefit in various types of disorders which require circulatory support. (Supported by Grants HE 12287, USPHS K3 GM 17, 651 and John A. Hartford Foundation.)

HOLOGRAMS OF MOVING RED BLOOD CELLS, M.O. Breitmeyer and M.K. Sambandam, 228

Rose Polytechnic Institute, Terre Haute, Indiana.

The photographic record of red cells suspended in normal saline has been made in order to investigate their orientation as they move toward the orifice of an electronic cell sizing system. Gabor's in-line holography in the Fresnel region was used. The illuminating source is a $6\,\mu$ sec graphy in the Fresnel region was used. The illuminating source is a pulse from an argon laser (TRW-83A). An image resolution of $2\,\mu$ was obtained by recording the Fresnel hologram of a micrometer scale. The reconstructed images are viewed under 200 X magnification, using a high resolution microscope. Ten film strips containing a total of 111 exposures were analyzed for three types of orientation (see figure). was found that 363 out of 839 cells counted (43.4%) had orientation (1), 355 (42.4%) in (3), only 121 (14.2%) in orientation (2). Results can be compared to those predicted by hydrodynamic theory. This principle of microholography should find applications in the study of capillary dynamics, wall-collision of cells and other areas of physiology.

Cell

Cell Orientation (1) (3) Cross section of orifice

SIMULTANEOUS PRESSURE MEASUREMENTS IN RENAL TUBULES AND POSTGLOMERULAR VESSELS USING DUAL SERVO-CONTROLLED CONTINUOUS RECORDING TRANSDUCERS. B.M. Brenner, T.M. Daugharty and J.L. Troy. VA Hosp. and Univ. Cal., San Francisco, California, U.S.A.

The servo-nulling transducer system described by Wiederhielm et al (Am. J. Physiol. 207: 173, 1964) was modified and assembled in duplicate to permit simultaneous and continuous micropuncture measurements of hydrostatic pressure (HP) in surface proximal tubules (PT) and surrounding peritubular capillaries (PC). PTHP (mean=14.3±0.6SE cm H2O) exceeded PCHP (mean=9.0+0.5) in each of 56 measurements in 12 hydropenic rats, with paired differences ranging from 2 to 10 cm H20. HP in parent efferent arterioles (mean=17.0+0.7 cm H2O) always exceeded branch PC; paired differences ranged from 4 to 18 cm H₂O. 19 simultaneous recordings of HP in proximal and distal tubules, usually of the same nephron, revealed the former to be uniformly higher, on average by 5.8 ± 0.6 cm ${\rm H}_{2}{\rm O}$ (range: 2 to 10). This gradient across Henle's loop was obliterated during strong osmotic diuresis. Elevation of HP in PT and PC (in the range of $20-50~\rm cm~H_2O$) induced by partial renal venous occlusion, mannitol diuresis or raised ureteral pressure yielded steady-state values for PT which continued to exceed PC (by at least 3 cm H2O) in 28/30, 32/37, and 34/37 instances, respectively. This persistence of a tubulo-capillary gradient suggests that quantitative inferences regarding Δ P across these structures from HP measurements in tubules alone are probably inadequate.

FILTRATE-FILTRAND RATIOS IN ULTRAFILTRATION ACROSS MEMBRANES AS AFFECTED BY THE PRESENCE OF ADDITIONAL SOLUTES. E.H. Bresler & George Green, VA Hospital, New Orleans, La.; R.P.

Wendt, Loyola University, New Orleans, La., U.S.A.

In determining the sieving characteristics of a membrane with respect to a given solute it is customary to work with binary solutions. The question arises as to whether the ratio of filtrate to filtrand concentration for a given solute will be altered by the presence of other solutes in a significant manner. Theoretical considerations suggest that if the sieving properties of the membrane are related to a dispersion of pore sizes marked effects can be observed. The ratio of filtrate to filtrand concentration for a 25 mM raffinose was studied for a Cuprophane membrane over a range of pressure 20 p.s.i. to 80 p.s.i. At above 40 p.s.i. the concentration ratio remained relatively constant at about 0.80. When 75 mMols of PEG-1000 were added and a filtration pressure of 50 p.s.i. applied, the concentration ratio approached unity. In other words, the membrane effectively ceased to act as a sieve for raffinose. This is not due to the reduction in flow rate as flow rates in the above described ternary system remained at levels which yielded concentration ratios of about 0.80 in binary mixtures. Thus, it appears that sieving of raffinose in cuprophane membranes is related to a dispersion of pore sizes. Under certain conditions bidirectional convective flows can occur in multicomponent solutions. It is suggested that this may at times be the case across biological membranes.

BIRD RESPIRATION: FURTHER STUDIES OF FLOW PATTERNS IN THE AVIAN LUNG AND AIR SACS. W. L. Bretz. Department of Zoology, Duke University, Durham, North Carolina, U.S.A.

The route of air flow in the avian lung and air sac system was studied in normally respiring unanesthetized mallard ducks. A marker gas (argon) was introduced via a tracheal cannula during a single inspiration, and the time of arrival of this marker was determined for the interclavicular, cranial thoracic, caudal thoracic, and abdominal air sacs. A time-of-flight mass spectrometer equipped with an atmospheric sampling system was riight mass spectrometer equipped with an atmospheric sampling system was used to detect changes in argon partial pressure in the air sacs. The marker arrived in the abdominal and caudal thoracic sacs, relatively undiluted, during the inspiratory phase in which it was introduced; it arrived in the more anterior sacs somewhat more diluted, during later expiratory and inspiratory phases. It appears that an inspired volume of gas initially flows to the posterior sacs, and only during subsequent phases of the respiratory cycle does this mass of gas flow to the anterior sacs, presumably through the bulk of the lung parenchyma. (Supported by NIH Postdoctoral Fellowship 1 F02 GMH3875-01.) 229

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CONTRIBUTIONS TO THE MATHEMATICS OF THE HYDRODYNAMICS OF THE INNER EAR.

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German Fed. Rep.

Similarities and differences in the mathematical treatment of the hydrodynamics of the inner ear as developed so far by Ranke, Zwislocky, Fletcher, Huxley and Petersen and Bogert are compared in detail. On this background mathematical models were programmed for the computer. The results are illustrated by a film. In addition examinations are done on the question, how far an analysis of frequency and difference limen for frequency is possible on the basis of the physical conditions in the inner ear provided the given anatomical dates are numerically taken into account. Furthermore a new mathematical model of the cochlea will be presented.

CROSS-BRIDGE PROPERTIES DERIVED FROM MECHANO-ENZYMIC EXPERIMENTS ON FIBRILIAR MUSCLE. W. Breull, J.C. Rüegg, G.J. Steiger, M. Ulbrich.
Inst. of Cell-Physiology, Ruhr-University, Bochum, German Fed. Rep.

Studies on the mechanics, ATPase activity and P.-ATP-exchange of iso-lated contractile structures (glycerinated fibres) from insect fibrillar flight muscle suggest a cyclic cross-bridge mechanism involving about 100 A bridge movement at 7 Hz (Lethocerus maximus, 20 C) or 12 Hz (Lethocerus annulipes, 20 C). In each cyclic operation of the bridge two ATP (Initial burst) or one ATP (steady state) are split into ADP, presumably via an 'energy rich' ADP-myosin passing into the myosin ADP complex described by Taylor, Lymn and Moll (Biochemistry 9, 2984 (1970)). A rise of temperature (Q 3.5) or phosphate concentration increases the frequency of cycling and hence that of isometric oscillations, the contraction speed and the enzymic turnover number of the actin activated ATPase. ADP has the reverse effect (competitively antagonized by ATP), while calcium ions and direct mechanical activation by stretch do not affect speed but increase tension by "cross-bridge recruitment" (rather than by enhancing cross-bridge turnover-frequency) in insect as well as in heart and skeletal muscle.

"UPTAKE AND DISTRIBUTION OF 32p IN THE RAT NEURAL LOBE IN VIVO". Bridges T.E. & Lederis K. Division of Pharmacology and Therapeutics, The University of Calgary, Alberta, Canada.

In an investigation of incorporation of 32p into membranes of hormone granules in the posterior pituitary it was recently found that, after intraperitoneal injection of 32p the neural lobe (NL) took up 32p at a considerably higher rate than either the hypothalamus (H) or the frontal cortex. In present experiments 32p uptake into the rat H and NL was measured at 1,4,12,24,48,72,96 and 120 hours after administration of 40pCi (10p1) of 32p into the 3rd ventricle. Incorporation into the NL reached a peak at 48 hours (22.1±4.5% of injected p32 per g. tissue; 5 rats) and had declined significantly at 120 hours (6.5±0.8%; 5). Uptake into H was maximal at 4 hours (61.9±5.9%; 5) and declined steadily throughout the experiment. In the first 48 hours, the amount of label appearing in the NL was identical with that disappearing from H. A large proportion of the 32p (60-90%) in NL and H was recovered in the acid-soluble fraction (AS) and the time course of uptake into AS resembled that into the whole tissues. Uptake into phospholipids (PL) (9-25% total) did not follow the same pattern, reaching a maximum at 24 hours and beginning to decline at 120 hours in both NL and H. Uptake into acid-insoluble, non-lipid was low (2-8%) and variable with time. It is concluded that the uptake pattern of 32p into NL after intraventricular injection differs from that after i.p. administration and may represent axonal transport of labelled compounds from H. In a similar experiment using rats previously dehydrated by replacing drinking water with 2.5% NaCl for 2 days, a reduced overall uptake of 32p into NL was found compared to controls with no change in the 32p uptake into phospholipids.

EFFECTS OF ALTERED MEMBRANE POTENTIAL ON THE FLUXES OF SODIUM AND POTASSIUM ACROSS THE SQUID AXON MEMBRANE. F. J. Brinley, Jr. and L. J. Mullins. Dept. Physiol, Johns Hopkins University School of Medicine & Dept. Biophys, University of Maryland School of Medicine, Baltimore, Md. 21201, U.S.A. Using a dialysis tube with a 25 µ Pt-Ir wire in its lumen so that currents could be smalled to the length of Theorems and the property region.

Using a dialysis tube with a 25 μ Pt-Ir wire in its lumen so that currents could be applied to the length of membrane outside the porous region, squid axons were dialyzed by a technique previously described. Dialysis medium was mainly K-D-aspartate with appropriate amounts of Na, ATP, and buffer. Na influx was measured both at a normal membrane potential and at one hyperpolarized about 30 mv. During hyperpolarization, Na influx was increased somewhat but this change was irreversible and persisted when hyperpolarizing current was removed. Experiments with Na efflux showed that it was largely unaffected by hyperpolarization nor was it affected if most of the K+ in the fiber was replaced by Tris+. Under such conditions membrane potential was near zero yet Na efflux that depended on ATP was virtually normal. Experiments with K efflux showed that it was reduced many fold by hyperpolarizing currents with K influx was unaffected. The conclusions from this study are that active transport fluxes seem to be unaffected by changes in membrane potential of from zero to 90 mv, although the thermodynamic work required for transport at these two potentials differs greatly. [Aided by grants from U.S. NIH (NS 5846 & GM 8427) and U.S. NSF (GB24585).

THE NATURE OF INTERACTION BETWEEN ATP AND ATPASE IN MICRÓSOMES. William A. Brodsky and Adil E. Shamoo, Mt. Sinai Sch. of Med. of City Univ. of N.Y. and Inst. for Med. Research and Studies, New York, New York, U.S.A.

Microsomes of turtle bladder epithelial cells contain a Mg dependent, Na + K stimulatable, ouabain-inhibitable ATPase. Incubation of the microsomes at 0°C with $\text{U}-1^{4}\text{C}-\text{ATP}$ and/or $\gamma-3^{2}\text{P}-\text{ATP}$ (0.01-0.3mM) resulted in the formation of 1^{4}C and/or $3^{2}\text{P}-\text{labelled}$ protein, wherein the amount of the carbon complex was 1/5 that of the phosphate complex. The pre-formed $1^{4}\text{C}-\text{protein}$ was proven to be an E-ATP complex, because ATP accounted for 80% of the 1^{4}C eluted into the supernatant at low pH levels. The amount of native E-ATP formed during incubation is unchanged by Mg, Na, K, or ouabain, but the amount of ouabain-treated E-ATP formed is reduced by addition of Na + K together. After hydroxylamine treatment at pH 7.0, the $1^{4}\text{C}-\text{bound}$ and the Na increment of $3^{2}\text{P}-\text{bound}$ are cleaved from the acid precipitated microsomes. The pattern of E-ATP formed versus pH was similar to the corresponding pattern of the sodium-induced increment of phosphoprotein formed. Treatment of the microsomal precipitates at pH 4.0 with pyridine, histidine, imidzole and methanol produced no change in the amount of bound 1^{4}C or 3^{2}P . The bond between the enzyme and ATP, as well as that between the Na form of the enzyme and phosphate has properties similar to those of acyl bonds. The pH profile of the Na-induced $3^{2}\text{P}-\text{binding}$ is qualitatively similar to the mucosal pH profile of sodium transport in the intact bladder. (Supported by NIH and NSF)

THE IMPORTANCE OF GROWTH HORMONE IN NORMAL LUNG GROWTH. J. S. Brody and W. J. Buhain.

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To investigate the influence of growth hormone (GH) on lung growth, we made

physiologic, morphometric and biochemical measurements of the lung in rats following hypophysectomy (HX) performed at 2-3 wks of age ("young rats") or at 7 wks of age ("old rats"). In "young rats" total lung capacity (TLC) was 4.8 ml at the time of HX, 5.1 ml at 6 wks of age (64% of normal controls) and 5.5 ml at 10 wks (43% of normal). Compared to controls of similar age, 3 wks after HX there were significant differences in: lung weight, 0.59 vs. 0.79 gms; number of lung cells (measured by total lung deoxyribonucleic acid - DNA) .86 x 106 vs. 1.14 x 106 cells; lung cell size (measured by ribonucleic acid/DNA ratios); and number of alveoli, 14.0 x 106 vs. 21.7 x 106 alveoli; but no change in alveolar size. Thus lung growth in "young rats", characterized by proliferation and enlargement of lung cells with formation of new alveoli, was prevented by HX. In "old rats", TLC was 10.6 ml at the time of HX, 9.0 ml at 10 wks of age (63% of normal) and 9.5 ml at 13 wks (58% of normal). Compared to controls, after 3 and 6 wks, there were significant differences in lung weight, number of lung cells and alveolar size, but no differences in lung cell size or number of alveoli. Lung growth in "old rats", characterized by cell proliferation and alveolar enlargement, was also prevented by HX. Exogenous GH completely or partially corrected these changes in both "young" and "old" rats. Our studies show that GH is important in normal lung growth in the rat, and suggest that both formation of new alveoli and enlargement of alveoli are growth hormone dependent processes.

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238 ACTION OF β-BLOCKING AGENTS AND AMIODARONE ON HEART WORK AND CARDIAC OUTPUT J.Broekhuysen and M.Ghislain. Labaz Research Center. 1120 Brussels. Belgium.

 β -Adrenergic blocking agents (βBA) are widely used to control arrhythmias and, at high doses, to decrease heart oxygen consumption (QO_2) in patients with angina pectoris. The QO_2 decrease is due to diminished cardiac work in parallel with a fall of cardiac output. Such a fall is ascribable to the decrease of both heart rate and stroke volume by βBA . Stroke volume is a function of the force of the contraction and of its duration, and βBA decrease the former. Cyclic-AMP has been claimed to increase Ca efflux from sarcoplasmic reticulum, and hence to increase strength of contraction; it is also known to stimulate glycogenolysis by activating the phosphorylase system. Cyclic-AMP concentration being held low by βBA , Ca availability will be lowered and the phosphorylase system inactivated, leading to progressive decreased cardiac output and increased glycogen stores. In the case of amiodarone, which is not a βBA , heart work and QO2 are actually reduced, but cardiac output is not. While partly counteracting the chronotropic effects of catecholamines and glucagon (and inducing bradycardia by itself), amiodarone decreases the speed of Ca uptake by isolated sarcotubular vesicles (though allowing higher plateau values) and hence increases the duration of contraction which adequately compensates for the decreased heart rate.

ELECTRICAL PROPERTIES OF VL THALAMIC NEURONES

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It is known that VL thalamic neurones driven by cerebellar and/or pallidal outflow show EPSP-IPSP sequences to stimulation of the intralaminar thalamic nuclei. The inhibitory component of this sequence has been shown to be frequency dependent (Broggi G. and Margnelli M., Brain Res., in press). This study was designed to investigate the membrane properties of these VL neurones. All experiments were performed on unanaesthetized encéphale isolé cats locally anaesthetized with xylocaine. Measurements of cell membrane resistence were obtained using the Wheatstone bridge technique on cells impaled with single glass microelectrodes filled with 2.2 MK-citrate. The vast majority of the cells studied showed linear I-V curves to inwardly, hyperpolarizing, and outwardly, depolarizing, applied current pulses. Only a small percentage of cells showed non linear behavior and this was in the direction of anomalous rectification. No differences in synaptic connections were observed for these cells.

The preliminary results indicate that the frequency dependency of the EPSP-IPSP sequence of VL neurons is not obviously related to any unusual electrical properties of their cell membrane and would seem to depend upon synaptic connections.

240 EXPERIMENTAL ANALYSIS OF CEREBELLAR DYSFUNCTION. V. B. Brooks, I. Kozlovskaya, A. Atkin, F. E. Horvath, and M. Uno. Dept. of Physiol., New York Med. Coll., New York, N.Y. USA.

Brief cooling of the dentate nucleus to the range of 20° to 10°C produced reversible dysmetria in performance of a step-tracking task that required accuracy of movement and holding without prescribing force or velocity. Three Cebus monkeys, implanted with cooling probes, were trained to move an unloaded handle through a horizontal arc between two targets, with alternating extensions and flexions about the elbow joint. Analysis of over 2,000 movements showed that <u>loss of velocity control</u>, characterized by excessive velocities reached through increases in magnitudes and durations of accelerations and corresponding decelerations, was a cause of dysmetria produced by cooling. The animals could regain successful, accurate target approaches by shifting from single complete movements made at high speeds to slow discontinuous stepwise movements, used even in subsequent control trials. However, amplitudes, peak velocities and velocity changes of the constituent steps during cooling still exceeded those of steps in control movements; i.e. during cooling constituent steps lacked velocity control as did single complete movements. Cooling delayed onset of antagonistic muscle action and reduced co-contraction, even in compensated stepwise movements. Normal movements returned in a few minutes after cooling. The effects described above were not obtained in equivalent movements from three monkeys during cooling of the interposed nuclei. Supported in part by USPHS Grants NS-05508 and NS-05544, and NSF Grant GB-8018.

EFFECT OF FOOT-UP TILT ON FOREARM VASCULAR CAPACITY. E. Brown, R. H. Edmund, P. Hutchins. Cardiovascular Res. Inst. and Dept. of Med., Univ. of Calif., San Francisco, Calif. USA.

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Raised blood flow in inferior vena cava and lowered forearm vascular resistance (R) continue during foot-up tilt after blood shift is complete (Pentecost et al., Clin. Sci. 24, 149, 1963; Roddie et al., J. Physiol. 139, 369, 1957). Little is known about behavior of capacitance vessels with this stress which shares some components with exercise and immersion. We raised hips and legs of healthy young men on a board tilted 45° to 52° above horizontal (heels 72 to 89 cm above heart) and observed pressure in unrestricted vein of forearm below heart level (VP), pressure in isolated occluded vein (VPO), and, by Whitney gage, forearm blood flow (FBF) and volume of forearm (FV) at various transmural venous pressures (TMVP) induced by congesting cuff and forearm pressure box. During tilt, FBF usually rose (average 34%, SD 46, N = 18); pulse and arterial pressure changed little. VP rose 3 to 10 mmHg and FV (free, at heart level) expanded accordingly. Raising TMVP very slowly from 0 to 30 mmHg during tilt caused increase in FV (V30) averaging 90% of control (range 66 to 106, N = 8). Usually VPO went up while forearm at TMVP 30 shrank (average -0.22% FV); but both effects were transient and less than after deep breath. FV at TMVP near 0 usually increased during tilt. Effects of decreased R on TMVP of capacitance vessels upstream to large veins may have contributed to the decreases in V30, and venoconstriction may not participate regularly in limb vascular response to stress of this severity. (Supported by USPHS Grant HE-06285.)

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TWO STABLE STATES OF A SINGLE PHOTOPIGMENT UNDERLYING THE RECEPTOR POTENTIALS IN LIMULUS MEDIAN OCELLUS. J. E. Brown and J. A. Nolte, Dept. of Biology, M.I.T., Cambridge, Mass. U.S.A.

The median ocellus of <u>Limulus</u> has two populations of photoreceptor cells which differ in the spectral sensitivities of their depolarizing receptor potentials: one peaks at 360 nm (<u>UV</u> cells), the other at 525 nm (<u>Vis</u> cells). With steady illumination by a bright 360 nm stimulus, the membrane voltage of a UV cell remains steadily depolarized. If a steady, long-wavelength stimulus is superimposed on the steady UV illumination, the membrane voltage hyperpolarizes. This "repolarization" elicited by a long-wavelength light in the presence of steady UV light is graded with the intensity of the stimuli. Also, spikes can be elicited both from single cells in the ocellus and from the median ocellar nerve with UV stimulation. The spike frequency is graded with stimulus intensity and becomes steady with steady illumination. The spike frequency in the presence of a steady UV light is decreased by simultaneous illumination with long-wavelength light. The spectral sensitivity of both the "repolarization " and the decrease in spike frequency peaks at 480 nm. Thus, the repolarization phenomenon cannot arise <u>via</u> a synaptic mechanism (electrical or chemical) from the <u>Vis</u> cell population. We propose that this repolarization phenomenon arises from two states of the same photopigment. (<u>1.e.</u> rhodopsin and a stable intermediate photoproduct), both of which are coupled to the mechanisms which generate the light-induced changes in membrane voltage. Supported in part by N.I.H. EY00312 and EY00377.

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ELECTRON MICROSCOPY OF MUSCLE FIBRES IN EXTREME PASSIVE SHORTENING. L.M.Brown, H.Gonzalez-Serratos & A.F.Huxley, Dept.of Physiology, Univ.Col.London and Ctr. de Investigacion y de Estudios Avanzados del I.P.N., Mexico 14 D.F.

Isolated frog muscle fibres can be shortened to an apparent striation spacing of 1.6 μm by longitudinal compression in gelatine. The sarcomeres shorten by sliding to a length S_{\min} ; further shortening is by bending of the fibrils. In some fibres $S_{\min} = 1.95~\mu m$ (the length of the thin filaments in vivo calculated from the X-ray periodicity of 385%); in others it is larger (up to 2.1 μm). In T.S., no fibre showed a double array of 12 thin filaments at the M line; in fibres with $S_{\min} > 1.95~\mu m$ the single hexagonal array

was not complete. In L.S., the sarcomeres in the wavy fibres were always as long as, or longer than, the thin filaments. Thus, in passive shortening the sarcomeres never shorten beyond the point where the thin filaments meet each other, and there is a variable amount of additional resistance to shortening, which in some cases makes the fibrils bend before the thin filaments meet.

THE CARDIOPULMONARY RESPONSE TO EXERCISE FOLLOWING PHYSICAL TRAINING IN AMPUTEES WITH VASCULAR DISEASE. A PRELIMINARY REPORT. I. Bruderman, T. Najenson, C. Gelbard, M. Serepka and P. Solsi. Pulmonary Res. Lab. Meir Hosp. Kfar Saba and the Loewinstein Rehab. Hosp. Raanana, ISRAEL.

Five male patients, aged 55 to 75 years with peripheral vascular disease underwent a 5-week program of progressive exercise training. All were one-leg amputees. The exercise consisted of: ball handling, light weight training and daily wheel-chair racing for speed and endurance. Before and at the end of the 5-week exercise training period the following cardiopulmonary parameters were measured at rest and following 5 minutes of standard submaximal exercise: heart rate, systemic blood pressure, oxygen consumption, respiratory minute ventilation, wasted ventilation, arterial Po2, PCO2 and pH. The exercise consisted of push-pull hand movements of 6 kg weight to one meter height at a constant rate of 44 movements per minute. After 5-weeks of training the same amount of exercise resulted in: a) slight decrease in heart rate, oxygen consumption and respiratory minute ventilation, and b) a marked decrease in wasted ventilation and a reduced increment in diastolic blood pressure as compared to the marked increase before the training. These results suggest that exercise training of the arms can improve the working capacity and increase the cardiopulmonary efficiency in aged patients with peripheral vascular disease.

Gastric secretion following sympathectomy in cats. Walter L. Brueckner, H. Loeweneck, F. Brendlein and F. Holle. Dept. of Surgery, Chir. Univ. Poliklinik,

Munich, Germany.

Although gastric secretion has been of interest to physiologists for over a century, scant information has been obtained regarding the influence of the sympathetic system on gastric secretion. A new method was developed in order to study gastric secretion more accurately following sympathec—tomy: By means of a dissecting microscope we stripped the sympathetic nets around the four gastric arteries and removed thus postganglionic fibers. In seventeen cats, some of them served as controls, we studied baseline and stimulated gastric secretion. Following results were obtained:

1) Baseline secretion: Following perivascular sympathectomy volume, total acid output and potassium concentration were unchanged. There was an increase of pepsin output (48 %).

2) Stimulated gastric secretion (with histamine): A significant increase of volume (33%), total acid output (56%) and pepsin output (47%) was observed

after perivascular sympathectomy. The differences are highly significant.

CENTRAL MECHANISMS IN THE MODULATION OF FLASHING IN LUCIOLA LUSITANICA. Bru-nelli, M., Fiore, L., and Magni, F. - Inst. of Physiology and CNR Laboratory of Neurophysiology, Pisa, Italy.

In female and non-flashing male fireflies brief photic stimulation evokes a flash with a latency of 200-300 msec which is followed by a prolonged (600 msec) depression to a second stimulus. The threshold of the flashing response to an electric shock applied to the brain is lowered by a preceding photic stimulus for 100 msec and is raised during the following 600 msec. Thus, in both sexes photic stimuli produce excitation followed by depression. In spontaneous flashing males, each flash is followed by a depression lasting about 900 msec; therefore within 900 msec the excitation induced by a photic stimulus remains without effect, whereas the depression summates with that associated with the spontaneous flash. When a photic stimulus is delivered to a flashing male 250-300 msec after a spontaneous flash, a high degree of summation of depression is attained; moreover both depressions come to an end simultaneously. As a result of postinhibitory rebound a male flash is driven with a latency of 600 msec. These findings provide an explanation for the flashing-dialogue, which is set up during mating behaviour.

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SLEEP-WAKING CYCLE IN THE ACUTE THALAMIC PIGEON. M. Brunelli, F. Magni, G. Moruzzi, D. Musumeci. Inst. of Physiology and CNR Lab. of Neurophysiology, Pisa, Italy.

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Spontaneous alternation between sleeping and waking behaviour may be observed in the <u>acute</u> thalamic pigeon, even within one hour after the operation. Short episodes of behavioural wakefulness interrupt the classical sleep syndrome several times during the day. The presence of a polyphasic sleep-waking cycle in the acute stage shows that Plourens' syndrome is not due to withdrawal of an influence of the cerebral hemispheres, but to surgical damage of the diencephalon, avoided with our technique. In the acute preparation light simply increases the time spent in wakefulness. Nociceptive stimulation of the awake bird is followed, after a few seconds of intense arousal, by sudden onset of behavioral sleep. The phenomenon recalls the displacement reactions described in the normal birds. In the acute thalamic pigeon the sleep response is predictable as any inhibitory reflex. As chronicity progresses it becomes more and more difficult to elicit the phenomenon, as if it were overwhelmed by the arousing effect of the nociceptive stimulation.

PITUITARY-ADRENAL CONTROL OF MEMORY. F.Robert Brush. Dept.of Medical Psychology, Univ.of Oregon Medical School, $\overline{Portland}$, \overline{Oregon} , U.S.A.

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Learning and retention of an instrumental avoidance response was studied in adrenalectomised, adrenal-demedullated, and control rats of both sexes. Adrenalectomy reduced the subsequent probability of learning in males but did not affect the females. Retention in control males was a U-shaped function of time, minimum at 2 hr., whereas that of females was inverted U-shaped function, maximum at 4 hr. Demedullation resulted in a monotonic decreasing function in both sexes, but adrenalectomy obliterated the retention function only in females. The results are interpreted in terms of demonstrated independent effects of adrenal corticoids and ACTH on retention.

EFFECTS OF TEMPERATURE AND TWITCH RATE ON FATIGUE IN FAST AND SLOW MOUSE MUSCLES.

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During 1/sec twitch activity tension output of excised, curarized, and massively stimulated fast gastrocnemius muscles first rises (treppe) and then falls. As temperature rises from 10 to 36 C treppe becomes greater and lasts longer but the mean rate of tension decline stays constant. Half-relaxation time (½RT) lengthens, but progressively less so as temperature rises from 10 to 24 C. Between 25 and 36 C ½RT shortens. At 25 C twitches at 2/sec cause the same tension changes as at 1/sec but they lengthen ½RT as in 1/sec twitches at 20 C. In fatiguing slow soleus muscles twitch tension never shows treppe, the mean rate of tension decline is ½ to ½ that of the gastrocnemius, and ½RT always shortens. Temperature and twitch rate have ne clear—cut effects on these changes. Fatigue shortens contraction time in both muscles regardless of temperature or twitch rate. The data partly suggest that in fast muscle the ejection of Ca⁺⁺ by the lateral cysternae is not exhaustive in a twitch and may be transiently enhanced during repetitive activity by higher temperatures (treppe). In fast, but not in slow muscle Ca⁺⁺ re-accumulation by the lengitudinal tubules apparently cannot keep pace with high twitch rates at low temperatures. Differences in speed and in temperature sensitivity of Ca⁺⁺ mevements may partly underlie differences in fatigue between fast and slow mammalian muscles.

250 EXPERIMENTAL AMBLYOPIA IN THE CAT. H.A. Ruchtel, G. Berlucchi and G. Mascetti. Inst.of Physiology, University of Pisa, Pisa, Italy.

We have attempted to produce uniocular amblyopia in ten cats by denervating the extraocular muscles of one eye. Subsequent visual discriminations were taught with both eyes exposed, then performance was tested using each eye separately. The eyes were equal in discriminating brightness but the immobilized eye was worse in discriminating patterns. In half the subjects the difference between the eyes was striking (200-500%). Immobilization per se cannot account for the results since learning with that eye alone was normal. Thus, it seems that in binocularly learned tasks, performance using only the immobilized eye was poor because information coming from that eye during learning had been suppressed by activity of the other eye. Experiments are now in progress to find the physiological mechanism for this suppression. Preliminary data showing that the ERG is the same for the two eyes suggest that the effect is indeed neural and not located at the receptor level. (Supported by NIH Research Grant 5 RO1 MH 15756-02 and Contratto CNR 70.01687/18).

251 CEREBELLAR RESPONSES TO STIMULATION OF THE VISUAL SYSTEM.
H.A. Buchtel, G. Iosif, G. F. Marchesi, L. Provini, and P. Strata, Lab. of Neurophysiology of the C. N. R. and Institute of Physiology, Univ. of Pisa, Pisa, Italy.

In cats without general anaesthesia the visual system has been activated both by natural stimulation (a flash in front of the animal) and by electrical stimulation of the optic chiasma and the superior colliculus. Evoked field potentials and unitary activity were recorded by means of glass micropipettes, mainly in Larsell's lobuli VI and VII.

The stimuli elicited field potentials which have been interpreted as beeing mediated by mossy fibre afferents. With electrical stimulation a later wave was sometimes observed, which has been interpreted as beeing mediated by climbing fibre afferents.

THE ACTION OF SEROTONIN ON INSULIN STIMULATED GASTRIC SECRETION, BLOOD GLUCOSE AND SERUM ELECTROLYTES LEVELS. J.Bugajski, J.Hano. Polish Academy of Sciences, Institute of Pharmacology, Kraków, Poland.

The mechanism of the inhibition by serotonin of the gastric secretion induced by insulin was investigated in cats and in rats with a chronic gastric fistulas. Insulin, 1 U/kg in cats and 1-5 U/kg in rats was injected intraperitoneally/IP/. Simultaneously serotonin, 1-10 mg/kg was applied IP, or 0.1 mg into lateral cerebral ventricles /IC/ in rats. The volume of the gastric secretion, the concentration and output of acid and pepsin was determined. Glucose levels of the blood, and the concentration of sodium, potassium and calcium ions of the blood serum was determined before drugs administration and every 1/2 -1 hour afterwards. Serotonin given IP or IC inhibited or significantly reduced gastric secretion but did not alter insulin hypoglycemia or hypokalemia. The inhibitory effect of serotonin on the gastric secretion stimulated by insulin is not related to the restoration of blood glucose and potassium ions levels.

EFFECT OF LEFT VENTRICULAR FILLING AND ADRENERGIC ACTIVITY ON MYOCARDIAL FIBRE LENGTHS.

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To assess relative changes in muscle fibre length, myocardial distances along the muscle bundles were continuously recorded by ultrasonic elements implanted in the left myocardium of dogs. Saline loading in anesthetized, open-chest dogs and in conscious dogs increased end-diastolic (EDMCL) and end-systolic myocardial chord length (ESMCL) in proportion to stroke volume (SV); myocardial shortening (MS = EDMCL - ESMCL) increased only slightly (Δ MS/ Δ EDMCL = 0.25) in control experiments and after propranolol administration. During infusion of isoproterenol or stimulation of the left stellate ganglion, MS increased. During subsequent saline loading at high and constant adrenergic stimulation, the further increase in MS was larger than in control experiments (Δ MS/ Δ EDMCL = 0.65). Similar ratios were obtained during mechanical lowering of SV. In intact, anesthetized dogs, the relationship between SV and end-diastolic ventricular pressure was not significantly different during saline and blood infusion. It is concluded that high adrenergic activity increases shortening of muscle fibres and better maintains end-systolic length during increasing end-diastolic length. Measurements at base and apex of the left ventricle could equally well be used for predictions of SV according to SV = k \cdot EDMCL \cdot ESMCL \cdot MS.

DOES 5-HYDROXYINDOLEACETIC ACID IN THE SPINAL FLUID DERIVE FROM BRAIN, BLOOD OR SPINAL CORD? M.Bulat and B.Živković. Inst. "Ruđer Bošković", Zagreb, Yugoslavia.

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5-Hydroxyindoleacetic acid(5-HIAA) in the spinal fluid is generally used as index of metabolism of 5-hydroxytryptamine(5-HT) in brain of neuro-psychiatric patients. However, this presumption is doubtful because the origin of 5-HIAA in the spinal fluid is obscure so far. We investigated this problem in cats. After intracisternal injection of 5-HIAA a long-lasting increase of 5-HIAA in the cisternal fluid, but no significant enhancement in the spinal fluid was observed. Penetration of 5-HIAA from blood into spinal fluid can be observed only when concentration of 5-HIAA in the blood is extremely elevated(this is not the case either in normal persons or in neuro-psychiatric patients). If metabolism of 5-HT in the spinal cord is altered by reserpine the changes of 5-HIAA concentration in spinal cord are followed by similar changes of 5-HIAA in the spinal fluid. We conclude, therefore, that 5-HIAA in the spinal fluid derives from metabolism of 5-HT in spinal cord. This shows that concentration of 5-HIAA in the spinal fluid cannot be used as index of 5-HT metabolism in brain as previously supposed.

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EVOKED POTENTIALS IN THE AUDITORY SYSTEM OF ALERT PORPOISES (CETACEA) AND SEA LIONS (PINNIPEDIA) TO THEIR OWN AND TO ARTIFICIAL SOUNDS. T.H.Bullock and S.H.Ridgway. Dept. of Neurosc., Sch. of Med., Neurobiol. Unit, Scripps Inst. of Oceanog., Univ. of Calif., San Diego and Naval Undersea Res. Dvlpt. Center, San Diego, Calif., USA.

Shafts carrying up to 18 electrodes were implanted into the brain of 9 Tursiops truncatus and 8 Zalophus californianus. Potentials were recorded and telemetered from the inferior colliculus or nucleus of the lateral lemniscus (cf. Bullock et al., Z. vergl. Physiol., 59:117-159 [1968]). The porpoises were trained to emit series of short clicks (0.06-1.5 ms long) on command, at 15-300 per sec., like those used in echolocation. Partly via conduction through the head, these cause evoked potentials. They were also used to trigger a test tone after a chosen delay, like an artificial echo. The potential evoked by the test tone can be 75% of its unconditioned height at 0.5 ms delay, and more than 90% at 1.0 ms. Both values are significantly higher than when conditioned by an artificial sound. These responses are highly specialized for brief (<0.1 ms) ultrasonic clicks (to >135 kHz); low frequency (<5 kHz), slowly rising tones (>2 ms rise time) evoked no potentials in the midbrain sites sampled but do in cerebral cortex. Sea lions show no such specialization but respond much like cats and not above 35 kHz.

VISCERAL AFFERENT PATHWAYS SYNAPTICALLY RELAYED IN THE INFERIOR MESENTERIC GANGLION OF THE CAT. I.A. Bulygin, V.N. Kaljunov, R.G. Lemesh. Inst. of Physiology, Byelorussian Academy of Sciences, Minsk, USSR.

Responses of the preganglionic trunks of the isolated and perfused ganglion to stimulation of the hypogastric nerves with single current pulses were recorded. Short latency response of direct fibres was often followed by the long latency wave which, unlike the first, was transmitted unidirectionally with a delay of about 6.5 msec in the ganglion and could be abolished by repetitive stimulation at 10-30/sec or by administration of pentamine or magnesium chloride. Conduction velocity of the second wave through postganglionic and preganglionic trunks was about 0.75 m/sec. These responses were especially pronounced in the nerves of aortic plexus. Conclusion was drawn of the existance of visceral afferent pathways synaptically relayed in the inferior mesenteric ganglion. Postsynaptic neurones of these pathways may send their axones both centripetally and centrifugally mainly through the nerves of the

POLE EVENTUEL DE L'AMP CYCLIQUE SUR LA CAPTATION DU D-XYLOSE PAR LE DIAPHRAGME ISOLE DE RAT HYPOPHYSECTOMISE SOUS L'INFLUENCE DE L'HORMONE SOMATOTROPE (STH) ET DES IONS CALCIUM. J.J.Buneaux, J.-C.Gounelle et Y. Raoul. Lab.de Physiologie, Faculté de Pharmacie, Paris 6e, FRANCE.

L'emploi d'inhibiteurs (théophylline) ou d'activateurs de la phosphodiestérase (méthyl-2-imidazole) montre que l'AMPC est un intermédiaire possible de la STH durant sa phase positive initiale d'action sur la captation du D-xylose par le diaphragme isolé de rat hypophysectomisé. Son intervention dans la phase secondaire de dépression de la captation de ce glucide reste hypothétique. L'addition d'ions Ca++ au milieu d'incubation réduit la captation du D-xylose. L'EDTA et l'imidazole l'augmentent en l'absence de Ca++; en présence de cet ion aucun des complexants essayés ne modifie cette captation, sauf le méthyl-2-imidazole. Malgré son action déprimante propre, le calcium semble favoriser durant la phase initiale les actions des associations STH-théophylline et STH-méthyl-2-imidazole.

DRUG INDUCED FACILITATION OF THE TRANSCOMMISSURAL INFORMATION FLOW IN RATS. O. Burešová, J. Bureš. Inst. Physiol., Czechoslovak Acad. Sci., Prague.

As shown by Giurgea UCB 6215 (Piracetam) selectively increases the amplitude of callosal evoked potentials without affecting direct cortical responses and primary responses. In an attempt to find the behavioural counterpart of this electrophysiological finding the effect of Piracetam on various forms of interocular and interhemispheric transfer was studied. Piracetam treated rats learned a pattern discrimination faster than controls both under monocular and binocular conditions. Monocular learning under Piracetam generated a much stronger secondary memory trace in the ipsilateral hemisphere than in control rats. The savings found during cortical spreading depression (CSD) in the hemisphere contralateral or ipsilateral to the trained eye were 68% or 38% in the untreated and 70% in the treated animals. Piracetam also facilitated interhemispheric transfer of lateralized visual engrams. Whereas in normal rats 5 interdepression trials with the naive eye did not elicit significant transfer of the engram previously formed under unilateral CSD, they induced in Piracetam treated rats 45% savings, revealed by retention testing under CSD in the trained hemisphere. The results indicate that Piracetam facilitates the transcommissural write-in mechanisms activated during monocular training or during transcallosal read-out of a lateralized trace.

TIME LABELLING OF INDEPENDENTLY ACQUIRED LATERALIZED ENGRAMS. O. Burešová, D. Goldowitz.Inst.Physiol., Czechoslovak Acad. Sci., Prague, Czechoslovakia.

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Sequential acquisition of two conflicting experiences leads to reversal. If the same habits are stored during unilateral cortical spreading depression (CSD) separately in the two hemispheres, acquisition of the second one is not accompanied by inhibition of the first one and the time labelling of the respective memory records is weakened. Functionally hemidecorticate rats were trained in a T-maze with the right hemisphere to go right and 24 hours later with the left hemisphere to go left. Free choice with both hemispheres intact revealed prevalence of the last experience when both engrams were of equal strength. Increasing the strength of the first habit and/or decreasing the intensity of the second habit stressed the importance of the first experience until finally the right and left choices were equally frequent. Thus 9/10 avoidances + 30 overlearning trials to the right were equilibrated by 3/3 escapes to the left. Control rats trained only the second habit retained it well (73.3 left choices) and animals learning the two tasks succesively with intact brain showed clear-cut reversal (86% of left choices). Correct time relationships of the lateralized records could be restored by a highly emotional intact brain experience(30 min.swimming)inserted between the two hemidecorticate learning sessions.

EXCITATORY PROPRIOSPINAL PATHWAY ASCENDING FROM LUMBOSACRAL TO CERVICAL SEGMENTS IN THE CAT. H. v.d.Burg, F.G.A. v.d.Meche, S. Miller, D.J. Reitsma and P.C. v.d.Velden. Dept. of Anatomy, Med. Fac., Rotterdam. The Netherlands.

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Coordination of movements of hind- and forelimbs is assumed to be mediated in part by long propriospinal pathways. In cats spinalized at C₁ under Flouthane anaesthesia electrical stimulation of hindlimb nerves evokes a discharge in the motoneurones of pectoralis major and latissimus dorsi, the ipsilateral hindlimb nerves being more effective than the contralateral. On reflex testing hindlimb facilitation of forelimb reflexes has a 5-12 msec onset and 10-25 msec duration. By contrast there is seldom any discharge or facilitation evoked in the more distal forelimb muscles supplied by the radial, median or ulnar nerves at the elbow. In the T₀ segment the pathway lies ventrally in the lateral funiculus and may therefore correspond to the long ascending propriospinal projections to motoneurones shown anatomically (Giovanelli Barilari & Kuypers. (1969). Brain Res. 14, 321.). It is suggested that this pathway may play a role in the coordination of hindlimb and forelimb movements such as stepping and jumping.

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ENDOCRINE GLANDS OF HYDROSALINE HOMEOSTASIS DURING GARDENDORMOUSE'S HIBERNATION.

C. BURLET, J. MARCHETTI, M. BOULANGE and E. LEGAIT. Lab. of Histology and Physiology, Univ. Med., NANCY, FRANCE.

In the gardendormouse (Eliomys quercinus L), the evolution of the endocrine glands playing a role in the hydrosaline homeostasis (hypothalamo-hypophyseal system with ADH and glomerular zone of the adrenal cortex with aldosterone) was studied during the animal cycle. (1) These glands don't follow the same evolution as that followed by other endocrine organs. (2) In the first phase of hibernation, the hypothalamo-hypophyseal system shows periods of hypoactivity separated by phases of hormonal release and synthesis. Histological, metrical, histoenzymological, biochemical studies and hormonal dosages demonstrate a state of hyperactivity. At the end of hibernation, the content of the neurohypophysis in ADH is higher than that before the sleep. (3) The histological and enzymatic characteristics of the adrenal glomerular zone show an important activity during the winter sleep. It il possible that the release of ADH plays a role on the spontaneous awakening in mammals'hibernation

PHYSIOLOGICAL STRESS AND ADAPTATION RESPONSES TO REPEATED ACUTE ACCELERATION AND THEIR 262 CUMULATIVE EFFECTS. 1 R. R. Burton and A. H. Smith. Sch. Aerosp. Med., Brooks Air Force Base, San Antonio, Texas, and Univ. of Calif., Davis, Calif.

Groups of adult male Single Comb White Leghorn chickens were exposed daily to acceleration (centrifugation) of 2 or 3G for: 10 mins.; 1 hr.; 4 hrs.; 8 hrs.; 12 hrs.; 16 hrs.; 24 hrs. (continuous); or 0 time (controls). After approximately 5 months of this intermittent treatment (training), the birds were exposed to continuous accelerations of the same G force (intensity). Their degree of stress and adaptation of each bird was determined by survival and relative lymphocyte count criteria. Intermittent training exposures of 2G developed levels of adaptation in birds directly proportional to the duration of their daily exposure. Intermittent training periods at 3G, however, produced a physiological deterioration in birds receiving daily exposures of 8 hours or more. Adaptive benefits were found only in the 1 hour and 4 hour daily intermittent 3G exposure groups. Exposure to 3G produced an immediate stress response as indicated by a low relative lymphocyte count which returned to control (pre-exposed) values prior to the next daily acceleration period in the 10 min., 1 hr., and 4 hr. groups. This daily recovery period from stress was considered necessary for developing adaptation as opposed to deterioration for the more severe environmental (3G) alteration.

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STATUS OF THE PINEAL COMPLEX ANTI-GONADOTROPIN. F.M. Bush and H. R. Seibel, Anatomy Dept., 263

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Evidence that the mammalian pineal complex secretes some antigonadotropin (AGT) includes: association between human pineal teratomas and hypo- or hypergonadism; effect of injected bovine pineal extract on gonads and vagina of rats; effects of pinealectomy on ovarian weight of rats and on spermatogenesis of hamsters; relation between pineal weight of pregnant rats and oophrectomy or injection of estradiol; and relation between reproductive organ atrophy of blinded rats and hamsters and cervical ganglionectomy or pinealec-

Melatonin, serotonin, 5-methoxytryptophol, and arginine vasotocin are pineal compounds with AGT properties. Evidence for melatonin includes: effect of injected melatonin on ovarian weight, frequency of estrus, and HIOMT activity; effect of implanted melatonin on LH in rats; relation of pinealectomy on proportion of pars distalis cells that contain LH; lack of effect of pinealectomy on testosterone-induced testicular atrophy in rats; and presence of HIOMT activity in pinealomas of humans with depressed sexual function. Injected serotonin causes gonadal atrophy in rats; injected 5-methoxytryptophol causes reduction in ovarian weight and decreased estrus in rats; and injected arginine vasotocin inhibits the stimulatory effects of gonadotropin on mice ovaries and uteri.

Evidence for and againt these AGT properties is discussed and effects of blogenic amines, pinealectomy, blinding, parabiosis, and hemicastration on reproductive organ, hypophysis, and adrenal gland weights and thyroidal activity in male hamsters is decribed,

as is testicular esterase activity and microscopy.

THYROID FUNCTION AND IODINE METABOLISM IN THE BEAGLE USING 125 I AND 131 I.* L.K. Bustad, 264 S.A. Book, J.M. Fuller, J.M. Stone, O. Wilson, Terrance McGinnis, Gloria Flores and L. Kumagai. University of California, Davis, California 95616, USA.

Prior to a long-term evaluation of the relative effectiveness of 125 iodine and 131 iodine and X-irradiation on the thyroid gland in the beagle dog, studies were performed to define normal thyroid function in the maturing animal. Radioiodine uptake by the thyroid, its retention by the whole body and thyroid, and values for serum PBI, T_4 and free T_4 , and T_3 resin sponge uptake were determined. The peak thyroidal uptake of 9-17% generally occurred from 48 to 72 hr after oral administration of radioiodine when dogs were maintained on diet providing a daily level of 0.5 mg of iodide. Retention was best expressed by a series of exponentials, with a biological half-time of about 8 days for the first component and about 50 days for the second component. The total radioiodine body burden appeared to be 25-50% extrathyroidal, following equilibrium at 5-7 days post-administration.

^{*} Supported by US Atomic Energy Commission.

PRESSURE-FLOW CHARACTERISTICS OF RENAL TUBULES AS RECORDED WITH A COMBINED PRESSURE TRANSDUCER MICROPERFUSION SYSTEM. M. Butz, H.Lohfert, K.Hierholzer, with techn.assist.of Ingrid Lichtenstein.Dept.of Clin.Physiology, F.U. of Berlin, Germany.

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Free flow microperfusion and pressure recording were achieved by a system consisting of the valveless connection of a microperfusion pump, a miniature pressure transducer and a single capillary. Thus, besides the conventional recording of intratubular pressures, flow rate in tubules can be changed by test solutions under pressure control. With knowledge of the flow resistance of the capillary tip (recorded before and after micropuncture) it is possible to measure pressure-flow relationships. In the proximal convolution a linear pressure flow characteristic was observed (infusion rate 0-30 nl/min). The system also permits local application of drugs and simultaneous recording of alterated tubular resistance. 10%-mannitol (10 nl/min), furosemide (2.2x10⁻¹¹ M/min) and K-cyanide (3x10⁻¹⁰ M/min) were studied in antidiuretic rats. All 3 drugs which impair Na and fluid reabsorption in the downstream segment change intratubular pressure. A sudden pressure rise due to mannitol exceeded that of controls with indigocarmine stained saline by 20%. In contrast furosemide and K-cyanide caused a gradual increase; however furosemide showed a time delay of ca. 4 min.

E.K.G., CRITERION FOR EVALUATION OF PHYSICAL EFFORT CAPACITY ON CHILDREN V. Buzoianu., St. Ionescu and C. Vlad. Departement of Physiology. Faculty of Medicine. Bucharest. Romania.

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Stating out of the objective criterion for estimation of the physical posibilities of children represents one of the main purpose of physiology .Studying this matter on homogeneous groups of children which were previously submitted to an under maximum dosed effort a succession of E.K.G., criterion has been stated out in evaluation of the adaptability to the effort.

Variability of cardiac frequency as well as of P-Q,Q-T, intervation and the contract of the c

Variability of cardiac frequency as well as of P-Q,Q-T,intervals P and T wawes, of the jointing point (J), and so on..,during recovering period depends on the effort intensity, sex, age and somatic growth.

E.K.G., data show a better adaptability to the effort of the girls of an age of II-years than the boys of the same age; after the age of I3 the adaptability to the effort is better for boys.

MYOCARDIAL OXYGEN CONSUMPTION IN ISOMETRIC CONTRACTIONS ABBREVIATED BY QUICK RELEASE. K.Y.Byon. Physiological Institute, University of Freiburg, Germany.

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In order to correlate mechanical parameters with oxygen consumption, tension development during isometric contractions in rabbit or cat papillary muscles was interrupted by a small quick-release (about 10% of initial length) at various times after stimulation. From a constant initial resting tension successive quick-releases applied near the peak of contraction allowed sudden relaxation to less than initial tension, and the amount of oxygen consumed was the same as in a series of normal contractions; accordingly quick-releases during isometric relaxation did not alter oxygen uptake. In contrast quick-releases applied at some point on the rising phase of the isometric contraction curve reduced the additional oxygen consumption caused by mechanical activity in a parallel manner to the diminution in isometric tension. Any development of tension after quick-release was accompanied by an increase in oxygen uptake. The linear relationship between the magnitude of developed tension and the rise in oxygen consumption above resting level indicates that the tension attained during an isometric contraction determines the energy expenditure of mammalian cardiac muscle.

268 AFFERENT CONTROL OF CENTRAL RESPIRATORY NEURONES. ¹Ewa Bystrzycka, ¹A. Huszczuk,
²B. 5. Nail. ¹Neurophysiology Laboratory, rolish Academy of Sciences, Warsaw, Poland.
²Depts. of Physiology and Engineering Science, Oxford University, England.

The electrophysiological activity of medullary and pontine respiratory neurones is normally studied in animal preparations which are paralysed and artificially ventilated. This manoeuvre eliminates movement artifacts due to voluntary muscle contraction, and largely controls movements associated with lung inflation. However, it disturbs the normal pattern and respiratory phase and synchronization of afferent impulses from receptors in the lung and chest wall. The effect of this disturbance was investigated using rabbit preparations in which the electrical activity of one phrenic nerve was used to drive a servo-motor ventilation system as described by Huszczuk (Huszczuk, A. (1970) J. Paysiol. 210, 183r). This preserved the pattern and synchronization of ventilation with the animals own central respiratory rhythm. The phase of synchronization could be altered by first passing the phrenic signal through a tape recorder with separated 'record' and 'replay' heads - so allowing a variable time delay to be introduced into the servo-loop. Digital computer analysis of trains of impulses recorded from medullary respiratory neurones in these experiments showed that their activity - as characterized by the frequency distributions of interspike intervals and measures of serial dependancy, stability and regularity of discnarge - was strongly affected by changes in the time relationship between inflation of the animals lung, and its central respiratory rhythm.

269 BEHAVIORAL THERMOREGULATION IN THREE POIKILOTHERMS.

Cabanac M., <u>Jeddi</u> E., Lab. Physiol. U.E.R. Med. Sud Ouest, Univ. Claude Bernard, Lyon FRANCE.

A 200 cm long aquatic container was built, having a thermal gradient of 0°C to 40°C. In it the thermopreferendum of three poikilothermic species was studied, two teleost marine fishes Chromis chromis and Scorpena scorfa and one amphibian Rana esculenta. Chromis chromis (n = 36) and Scorpena scorfa (n = 36) were spread in the container from 8°C to 26°C but the greatest number were at 20°C. With Rana esculenta (n = 48) the preferred temperature was stricty limited between 25°C and 28°C. In control experiments, placed in the same container in the absence of a thermal gradient, the animals chose the extremities. This result increases the validity of the above findings. When introduced into the bath the animals immediately left extreme temperatures. This suggests the existence of a peripheral thermal sensitivity. It is likely though, that the behavior depends upon thermal messages from inside the body since 1) The further choice was not immediate, the animals stabilized progressively in their thermopreferendum in 30 to 45 minutes. 2) In Rana esculenta, (n = 7) internal heating with an insulated electric resistance implanted intra-abdominally, was repeatedly followed by a movement of the animals toward the cold water of the thermal gradient. Interruption of internal heating was followed by a return to the thermopreferendum.

PULMONARY CLEARANCE OF AMMONIA. R. Cade, R. Hunt, D. Williams, H. Ramsey, and E. Schlein.
Departments of Medicine & Aerospace Engineering, Univ. of Florida, Gainesville, USA.

Net addition of ammonia to body fluids occurs with deamination and deamidation of amino acids by the kidney and with bacterial breakdown of protein in the intestine. Although a small amount of arterial blood ammonia is excreted through the kidney by glomerular filtration; the major mechanisms for net removal of ammonia from the body are conversion to urea by the liver and excretion of NH3 by the lung. We have studied pulmonary clearance of ammonia in a group of normal humans, and in patients with cardiac, renal, and liver disease. Ammonia in dried expired air was measured at a wave length of 2046A utilizing a second-derivative spectrometer signal. Ammonia in mixed venous and arterial whole blood and plasma was determined by the same method after alkalinization to a pH of 13. Mixed venous and arterial pH and pCO2 were determined in samples of blood obtained simultaneously with those used for determination of ammonia. Expired air was collected into 10L polyethylene bags passing through a short warmed polyethylene tube, a warmed three way valve and a Na₂CO₃ desiccant. Pulmonary clearance of NH₃ in our subjects ranged between 0.55 and 6.5 ml/min. linear relationship between clearance of ammonia and arterial blood pH occured over a pH range from 7.29 to 7.50. Both metabolic and respiratory alkalosis markedly increase pulmonary excretion of NH_3 and rapidly lower blood ammonia concentration while respiratory or metabolic acidosis have the opposite effect. GLUCOSE LIMITED LACTATE FORMATION IN HYPOXIC ANESTHETIZED DOGS. <u>Stephen M. Cain</u>. USAF Sch. Aerospace Med., Brooks AFB, Texas, USA.

In other experiments (Cain, Am. J. Physiol. 217:110, 1969), the sympatho-adrenal response of anesthetized dogs to severe hypoxia appeared inappropriate because the calorigenic action of catecholamines caused increased demand for energy when aerobic metabolism was least able to supply it. Excess lactate was also shown to be the best correlate of the estimated energy deficit incurred during severe hypoxia. Instead of a standardized time of exposure to hypoxia as was used before, anesthetized paralyzed dogs were breathed on 9% O_2 in N_2 until mean arterial blood pressure (MAP) rapidly decreased, a sign of impending irrecoverability. Animals were restored to room air as MAP became less than 70 mm Hg, and recovery was followed for 2 hrs. Hypoxia time, net oxygen deficit (NOD), excess lactate (XL) and arterial glucose levels were measured or calculated. Hypoxia time ranged from 40 to 127 min (91 \pm 28, mean \pm S.D.), NOD from 79 to 229 ml/kg (130 \pm 50), and XL at the end of hypoxia from 4.8 to 13.3 mM (8.0 \pm 2.7). No apparent relationship was seen between tolerance time in hypoxia, NOD, or XL. XL was, however, very significantly correlated (P < .001) with arterial glucose levels at the end of hypoxic exposure: XL = 0.511(G) + 3.83; r = 0.953. This relationship did not exist during hypoxia before physiologic failure. Because the hypoxic endpoint was evidently not failure of cardiac function, the energy deficit which could be accumulated during hypoxia was probably limited by cerebral hypoxia and the dependence of the brain on glucose availability to supplement deficient aerobic energy production by anaerobic metabolism. The sympatho-adrenal response would thus be important in increasing glucose availability to the brain.

POSITIVE FEEDBACK OF OVARIAN STEROIDS ON THE RELEASE OF LH IN IMMATURE RATS L.Caligaris, J.J.Astrada and S.Taleisnik. Inst.de Invest. Méd. Mercedes y Martín Ferreyra, Córdoba, Argentina.

The release of LH (determined by RIA) was studied in immature rats. The administration of progesterone (P) three days after a single injection of estradiol benzoate (EB) induced release of LH a few hours later in female rats from the 22 days of age, but not in 20 day old animals. Up to the age of puberty (32 days), the concentration in serum LH was higher than that of the adult rats receiving the same treatment. From 32 days on, following ovarian steroid treatment, the serum LH values were similar in young and in adult animals. Ovariectomy soon after birth advanced the age of response in two days. On the contrary, administration of 0.5 µg EB 5 days after birth delayed the response. No positive feedback effect of ovarian steroids on LH release was observed in male rats. It is concluded that the mechanism responsible for LH release matures around day 22 of age and that estrogen has a delaying effect on this process.

FURTHER EVIDENCE FOR ACH TRANSMISSION IN THE COCKROACH CENTRAL NERVOUS SYSTEM STUDIED AT THE UNITARY LEVEL. J.J.Callec and J.Boistel. Lab.Physiol. animal., Unit.Sci.Biol., Univ.Rennes \overline{I} , $\overline{35}$ - France.

Excitatory synaptic influences from cercal mechanoreceptors were investigated in order to elucidate the transmitter involved on the giant fibre system in the sixth abdominal ganglion of the cockroach. The oil-gap method has been used to record the post-synaptic activity (Pichon & Callec; J.exp. Biol., 1970, 52, 257-265). ACh has been tested either on the whole ganglion or by electrophoretic injection in the vicinity of the dendritic tree of a giant axon. It gives rise to a depolarization accompagnied by an increase in the post-synaptic conductance. Nicotine applied on the whole ganglion gives action comparable to ACh one. d-tubocurarine (10-4 to 5.10-4 g/ml) blocks all excitatory inputs while Atropine has a less powerful effect. Anticholinesterases, such as Eserine, have a strong facilitatory effect at low concentration (10-8 to 5.10-8 g/ml). Eserine prolongs and enhances as well ACh-depolarization as the EPSP. It is concluded that the presumed transmitter is ACh for all excitatory inputs and that the cholinergic postsynaptic receptors are probably of nicotinic nature.

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274 "INFLUENCE OF AGE IN THE ENERGETIC BALANCE IN PIGS OF IBERIAN TYPE".

A. Calleja, J. Boza and G. Varela. - Dept. Animal Physiology. - Estación Experimental del Zaidín. - Granada. Spain.

We have carried out five experiments of energetic balance in - "Iberian" type pigs,3,4,5,6 and 7 months old. The energy of the diet, - foeces and urine has been determined by a calorimetric pump. The samples of urine have been lyophilized before their combustion in the pump. The mean results expressed as the percentage of energy retained of the energetic intake were the following:

The statistic treatment shows that the retention of energy is - significatively higher (P 0,1 %) during the 5th and 6th months than during the previous ones, coming back to its initial values when it reaches the 7 months age.

MLMBRANE POTENTIAL TRAJECTORIES UNDERLYING MOTONEURON FIRING RATES. William H. Calvin and Peter C. Schwindt. Departments of Neurological Surgery and of Physiology/Biophysics, University of Washington School of Medicine, Seattle, Washington 98105, U.S.A.

Injecting a constant current into a cat spinal motoneuron causes the cell to fire repetitively, mimicking synaptic drive. The initial firing rate adapts to a lower steady rate after a small number of spikes. For both rates, the plot of firing rate vs. injected current (the f-I curve) is linear over two regions: The primary range and a steeper secondary range for high currents. This study focuses upon the membrane potential trajectory between spikes underlying these well-known input-output relationships. The secondary range has a characteristic, but complicated, trajectory. In the primary range, the voltage scoops downwards after a spike and then rises linearly to the firing level for the next spike. In some cells, the steepness of the linear rise (the ramp) is proportional to spike. In some cells, the steepness of the linear rise (the ramp) is proportional to spike does not change with current but the depth and time course of the preceding scoop alter with current to change the interspike interval. In still other cells, both scoop and ramp changes are seen. The decline in firing rate during adaptation to a constant current step is typically effected by an increase in the duration of the scoop, not ramp changes. Selected cells show adaptation due only to scoop increases and steady rate changes. Selected cells show adaptation due only to scoop increases and steady rate changes due only to ramp steepness, suggesting that the two descriptive types of trajectory change may indeed reflect different mechanisms controlling repetitive firing. [Supported by grants NB 04053 and GM 00260 from National Institutes of Health.]

276 SOME ASPECTS OF THE INFLUENCE OF SEROTONIN ON THE METABOLISM OF THE HYPOTHALAMUS RELATED TO SEX HORMONES. D.G.J.Campos and W. Ladosky.Dept.Physiology. Fac.Ciências Médicas, Univ. Católica do Paraná, Curitiba, Paraná, Brasil.

Serotonin decreases oxygen consumption by hypothalamic but not by cortical homogenates in the Warburg apparatus. This decrease is not related to sex, but it is observed in hypothalamic homogenates from castrated as well as from intact rats; as castration increases oxygen consumption, the inhibition is greater in the castrated as well as in the intent.

when pyruvate is used as substrate the inhibitory action of serotonin is observed not only in homogenized hypothalamus from castrated rats but from rats that were intact, castrated, injected with gonadal steroids or adrenalectomized. Neither citrate nor succinate oxidation are inhibited by serotonin in normal or castrated rats.

Oxygen consumption of male hypothalami is always higher than those of females and this difference is maintained even when substrates and/or serotonin were added. As castration does not modify the difference and it appears with any substrate used, it is suggested that it may be related to the process of sexual differentiation of the nervous system.

ASYMMETRICAL PROPERTIES IN ISOLATED TOAD LENSES. <u>O.A. Candia</u>, <u>P.J. Bentley</u> and <u>C.Mills</u>. Dept. of Ophthalmology, Mt. Sinai School of Medicine of the City University of N.Y. New York, N.Y. 10029 U.S.A.

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We have previously shown asymmetrical electrical properties between the anterior and posterior sides of the isolated toad lens. This asymmetry results in an overall PD of about 25 mv across the entire lens and a short-circuit current (SCC) of 30 ua/cm². We have further investigated other differences in the physiological behavior of these two surfaces. pH changes have a greater effect on the PD of the anterior side. While the lens is isolated in the chamber it looses K to the bathing solutions. In a 15 hr period the loss to the anterior solution is 58% larger than the loss to the posterior solution. Resistance measurements showed asymmetry at each surface. Resistance was 15% larger when positive current was sent into the lens from either bathing solution than when current was sent from the lens to the bathing solutions. SCC can be abolished by IAA and ouabain. However, the anterior but not the posterior side is sensitive to the action of these agents.

EQUILIBRIUM OF NUCLEOTIDES III STIMULATED FROG MUSCLES.P. Canfield and G. Maréchal Dept de Physiologie, Univ. de Louvain, Louvain, Belgium.

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Creatine (C), phosphorylcreatine (PC), ATP, ADP, AMP and IMP have been assayed in perchloric acid extract of 144 frog sartorius muscles (half of them being poisoned with iodoacetate). The muscles have been frozen at the end of one isometric tetanus (20C) before they could relax. The ratio C/PC increases with duration of stimulation, from 0.45 for resting muscle to 8.4 for iodoacetate poisoned muscles stimulated 12 sec. In a first approximation, the associated changes in ATP, ADP and AMP agree with a simple model: a) ATP and AMP are free in sarcoplasm, ADP is partly bound, partly free; bound ADP is taken as equal to ADP of resting muscle and is excluded from the enzymatic equilibrium; b) the ATP-PC transferase reaction has an in vivo equilibrium constant of 28; c) the myokinase reaction has an in vivo equilibrium constant of 2.5. However, when C/PC is in the range 2 to 6, ATP is higher and AMP is lower than predicted by the model. When C/PC goes over 2, an IMP production occurs which is always higher than AMP production; this suggest that deamination of AMP stabilizes ATP at a level higher than that predicted by a simple equilibrium model.

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PRESYNAPTIC INHIBITION OF SPINAL MOTONEURONES BY MUSCLE VIBRATION. A. Cangiano, B. Ghelarducci and O. Pompeiano. Istituto di Fisiologia, Cattedra II, Università di Pisa, Pisa, Italy.

This study was designed to dissociate presynaptic from postsynaptic inhibition in spinal motoneurones. Unanaesthetized spinal cats were used after anaemic decortication. The selective effects of repetitive discharge of Ia afferent fibres on primary afferent transmission in extensor monosynaptic pathways were studied by intracellular recording from ankle extensor motoneurones, during high-frequency (300/sec) sinusoidal stretch of the semitendinosus muscle. In 5 out of 19 cells the resting potential was unaltered by amplitudes of vibration up to 200 m, while the monosynaptic EPSP showed an average maximum depression of 30% (range 22-40%); repetitive firing induced by injected current failed to reveal changes in motoneuronal excitability. In the other cells slight inhibition of the repetitive discharge appeared during vibration, but small hyperpolarization was detected by computer averages of membrane potential. True inhibitory action contributed to this hyper polarization. It is concluded that appropriate experimental conditions allow to dissociate presynaptic from postsynaptic inhibitory events.

TUBULAR FUNCTION IN THE MESONEPHROS OF CHICK EMBRYOS.

K.Čapek, M. Kubát, Z. Friebová. Inst. of Physiology, Czechoslovak Academy of Sciences, Praha, Czechoslovakia.

A micropuncture study of chick embryo mesonephros was performed on the 7th,10th and 14th day of incubation.On day 5 the mesonephros was made accessible for puncturing and collecting samples both in superficial tubules and/or ductus Wolfi by a previously described surgical procedure.Sodium transport in different parts of the tubules and the effect of hormones thereon was studied using "Na and "C inulin.TF/P inulin,Na,K,t1/2,GFR and final Na and K concentration was measured.Age differences in the parameters measured were found indicating that Na transport is present at early stages of ontogeny and is responsive to humoral factors such as vasopressin and aldosterone.

TIME COURSE OF POTASSIUM CONTRACTURES AT LOW TEMPERATURE. Carlo Caputo, Dept. of Physiology, Univ. of Rochester, Rochester, New York, U.S.A.

Frog single muscle fibers were exposed to 190 mM K at low temperature (3°C) The contractures produced had a long plateau (c.15 sec) followed by a slow exponential relaxation phase (rate constant c 0.15 sec 1). The contractures could be cut short by suddenly lowering the [K]_o from 190 to 2.5 mM. After a contracture was cut short, reexposure to 190 mM K produced a redevelopment of tension. The period of interruption could be prolonged beyond the duration of the original contracture without affecting the second response. This second response was not due to repriming since at low temperature repriming was much delayed. For contractures cut short early during the plateau, the sum of the time integrals of tension in the two responses was equal to the time integral of tension in the uninterrupted contractures. A equal to the time integral of contractures cut short at the end of smaller value (84%) was obtained for contractures cut short at the end of smaller value (84%) was obtained for contractures cut short at the end of the plateau or later. These results can be explained by assuming that the release of the contractile activator occurs during most of the contracture duration. Release can be stopped by repolarizing the membrane and resumed by depolarizing it again. Addition of tetracaine or removal of external by depolarizing it again. Addition of tetracaine or removal of external by 2.5 mM K. In these cases, however, no tension was redeveloped when the standard 190K solution was reapplied.

4CTION OF ENDOOCULAR PERMEABILITY ANTAGONISTIC CATIONS, IN EXPERIMENTAL HYPOBARISM HYPEROPHTHALMOTONIA. M.Carapancea, C.Buşneag, L.Ciontescu, E.Udroscu. "D.Danielogolu" Institute of Normal and Pathological Physiology,
Rumanian Academy of Medical Sciences, Bucharest, Soc. Rep. of Rumania.

High altitude experimental hypobarism induces, in rabbit, an evident bilateral intraocular hypertension, concomitant with: (a) a very significant hyponatremia decreased by 41 mg%, accompanied by an also very significant increase with 41 mg% of the aqueous humor Na,(b) an insignificant hyperkaliemia accompanied by an also insignificant K decrease of aqueous humor, the latter modification appearing all the more important as sometimes K increase of aqueous humor amplifies the Na constant and major hydrophilous action, in this situation and (c) a very significant Ca increase, both in blood serum with 0,69 mg%, as well as in aqueous humor with 1,42 mg%.

Thus in experimental hypobarism, intraocular tension represents the resultant of endocular interference antagonism of the action of Na and K hydrophilous ions, which increase considerably aqueous humor permeability, with the action of Ca ion, which diminishes slightly this permeability, the mechanism mentioned having an tensio-intraocular homeostatic character.

INFLUENCE OF THE CEREBELLUM ON THERMOREGULATION REACTIONS. N.Cărare and A.Crîngu. Laboratory of Physiology, Faculty of Medicine, Iassy, ROMA-NIA.

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The authors investigated changes in the thermoregulating capacity in decerebellate animals. Experiments were carried out in controls and in dogs with complete removal of the cerebellum in which the thermoregulating capacity test was performed (3 hours' exposure to +6°C followed by 15 min exposure to +45°C). Thermic reactions induced by ambiant temperature variations were investigated both in vigile and in anesthetized animals and were correlated with electrocardiographic and respiratory modifications. The experimental data obtained showed that chronic decerebellate animals exhibit in the course of thermolysis at least a double elevation of central temperature as compared to controls.

RETINAL PRODUCTION OF ACTIVE METHOXYINDOLES IN MAMMALS. D.P. Cardinali and J. M. Rosner. I. L. A. F. I. R., Univ. del Salvador, Argentina.

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Hydroxyindole-O-methyl transferase (HIOMT), the enzyme responsible for the biosynthesis of melatonin and other endocrine active methoxyindoles, was studied in eyes of rats from fetal to adult life. This enzymatic activity increases from the 17th day of gestation (2.4 \pm 0.6 and 1.9 \pm 1.0 μh moles of melatonin/hr/both eyes in males and females) to the 30 th postnatal day, where it reaches a plateau (15.9 \pm 3.3 and 12.1 \pm 2.2 in males and females, respectively). After puberty a significant sexual difference in favor of the males was observed (p \langle 0.01). The enzymatic activity was exclusively located in the retina (105,000 g supernatant) and it was also found in retinas of guinea pigs and rabbits. The incubation of serotonin -2-14C with rat retinal tissue demonstrated the metabolization to N-acetylserotonin, hydroxyindoleacetic acid, hydroxytryptophol, melatonin, methoxyindoleacetic acid and methoxytryptophol. The presence of HIOMT in the retina is the first evidence that a tissue other than the pineal gland can biosynthesize endocrine active methoxyindoles in mammals.

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RECURRENT INHIBITION OF REFLEX RESPONSES IN THE FROG SPINAL CORD. $\underline{G.Carels}$ and $\underline{J.A.Cerf}$. Lab. of Neurophysiology, Fac. of Sciences, $\underline{Univ.}$ of Brussels, Belgium.

Antidromic excitation of a ventral root (VR) results in a dorsal root potential (VR-DRP) due to depolarization of primary afferent terminals. The antidromic volley is also followed after delay by an inhibition of reflex discharges initiated by stimulation of dorsal root or cutaneous afferent fibers, but not of the early VR potential evoked by stimulation of a muscle nerve. The presynaptic spike at the first internuncial relay of the reflex pathway is slightly reduced during the VR-DRP, suggesting a presynaptic mechanism for this recurrent inhibition. However, the depth of inhibition seems unrelated to the amplitude of the VR-DRP and their time courses usually differ. These discrepancies are temperature-dependent, and more pronounced after a conditioning tetanization of the VR. A full-sized VR-DRP is elicited by firing of low-threshold motor axons, whereas maximum inhibition requires stronger stimulation of the VR. Added to the observation that the inhibition, contrary to the VR-DRP, resists to picrotoxine and is abolished by strychnine (J. de Physiol. 58: 487, 1966), these results suggest that primary afferent depolarization plays only a minor part in the mechanism of recurrent depression of the reflex.

LONG-TERM HABITUATION OF SIPHON WITHDRAWAL REFLEX IN <u>APLYSIA</u>. T. Carew, H. Pinsker and <u>E. Kandel</u>. New York University Medical School, New York, N.Y., U.S.A.

Short-term habituation and dishabituation of the gill withdrawal reflex (GWR) have recently been described and their neural mechanisms analyzed. We now report long-term habituation of a related behavior, the siphon withdrawal reflex (SWR). This reflex can be measured in an unrestrained animal, thus permitting long-term studies. Animals were housed in individual aquaria and not handled throughout the experiment. Siphon was stimulated by a jet of sea water and the duration of SWR measured. Experimental group (N=19) received 10 trials/day (i.t.i.=30 sec) for 4 days. Control group (N=21) received no habituation trials. On Days 5 and 12 both groups received 10 trials using a blind procedure. In experimental group habituation occurred within each daily session and built up across days. On Day 5 duration of SWR was 20% of Day 1. This habituation persisted unchanged for at least a week (Day 12). Control group showed within-session habituation (Day 5) comparable to that exhibited by the experimental group on Day 1. Difference between experimentals and controls was statistically significant: Day 5, p<001; Day 12, p<01.

Long-term habituation of SWR resembles higher long-term learning in that spaced

Long-term habituation of SWR resembles higher long-term learning in that spaced trials (10/day for 4 days) produced significantly more habituation (p<.0001 on Day 5) than massed trials (40/day on Day 4). Since siphon stimulation usually also elicits GWR, these experiments offer the additional possibility of studying long-term habituation of a reflex whose neural circuitry is relatively well understood.

A CUMPARISON OF SENSORY BEHAVIOR AND THE ACTIVITY OF POSTCENTRAL CORTICAL NEURONS, OBSERVED SIMULTANEOUSLY, ELICITED BY OSCILLATORY MECHANICAL STIMULI DELIVERED TO THE CONTRALATERAL HAND IN MONKEYS. G. Carli, R. H. LaMotte, and V. B. Mountcastle, The Johns Hopkins University, Baltimore, Maryland, USA.

Our purpose was to observe what changes in the activity of postcentral cortical neurons can be correlated with an increasing liklihood of detecting somesthetic stimuli. We measured the performance of monkeys trained in a variable delay, reaction-time, paradigm to indicate when they detected vibrating mechanical stimuli (30 Hz, $0-50\mu$) delivered via a 3mm probe tip to the glabrous skin of their hands. The electrical signs of cortical neuronal discharges were recorded simultaneously by microelectrodes inserted into the postcentral gyrus via implanted, fluid-filled chambers. Cortical neurons were classifiable in terms of static and dynamic properties into groups, each thought to receive relayed primary afferent input from only one of the major sets of myelinated mechanoreceptive fibers of monkeys innervating the glabrous skin. A majority of that set of postcentral neurons linked to quickly adapting afferents was periodically entrained by the sine wave stimuli. Fourier analysis of cycle histograms showed that the amplitude and energy fractions of the first harmonic increased together with increasing stimulus amplitude, and reached significant levels at those amplitudes first detected. At the 50% level of detection the neuronal responses elicited by those stimuli detected differed in no obvious way from those missed. (Supported in part by USPHS Grant # 5P01 NSO 6828).

288 CHANGES IN NITROGEN METABOLISM OF THE SOUTHAMERICAN LUNGFISH KEPT IN WATER OR UNDER CONDITIONS OF WATER SHORTAGE. N.J.Carlisky and A.Barrio. Dept.de Quím.Biol.,Fac.Farmacia y Bioquímica, Univ.de Buenos Aires

The australian lungfish can not pass from water to land and the african variety isolates itself in land in an impermeable cocoon. This is not the case with the southamerican Lepidosirem paradoxa, suggesting that it could be a suitable animal to produce experimental changes of II metabolism similar to those which occurred in evolution in the passage from water to land. In water most of the excreted II was NH3 (63-88%) and the concentrations of urea in liver, kidney and muscle were 10 times lower than in animals kept out of it. In 117 and 356 days the hepatic synthesis of C14 urea from C14 HC03Na rose to 0.43 and 0.81 umoles/g-1/h-1 in animals kept out of water as compared with 0.1 and 0.13 respectively in those kept in water, while no urea was formed from C14 serine. This synthesis required acetylglutamate aspartate and ATP, it was inhibited by citrulline and was absent in the kidney. The actual tissue concentrations of urea in animals kept out of water were 3-4 times greater than those theoretically calculated. Both criteria indicate a sharp rise in the urea synthetizing capacity associated to the passage from water to land, which is an evolutionary antecedent of what is later observed in the metamorphosis of amphibia.

Na-EFFLUX AS A FUNCTION OF INTRACELLULAR Na CONCENTRATION IN CARDIAC PURKYNE FIBRES. E. Carmeliet and S. Bosteels. Department of Physiology, University of Leuven, Belgium.

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Intracellular Na content in cardiac Purkyne fibres of the cow was estimated from the slow phase of $\mathrm{Na}^{22}\text{-efflux}$. The extracellular phase was determined from the fast phase of Na^{22} -efflux or the equilibration space of mannitol, sucrose or inuline. Depending on the technique used the estimated intracellular Na concentration varied between $18.5 \ \text{and} \ 40.6$ mmole/1 intracellular water. The dependency of Na-efflux on intracellular Na content was determined in three types of experiments : 1) steady-state Na-flux, 2) netto Na-efflux (surplus Na-efflux) after preloading in K-free Tyrode and 3) netto Na-efflux in Na-free solution. In all cases Na-efflux was found to be directly proportional to the second power of the intracellular Na content, suggesting a reaction with the membrane carrier: 2 Na + X ≠ Na2X++.

METABOLIC CONTROL OF MEMBRANE PERMEABILITY IN APLYSIA NEURONS. David O.

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METABOLIC CONTROL OF MEMBRANE PERMEABILITY IN APLYSIA NEURONS. David O. Carpenter, S. William Snover and Jeffery L. Barker, National Institute of Mental Health, Bethesda, Maryland, USA.

The input resistance of the giant nerve cells of Aplysia varies between 10⁶ and 2 x 10⁷ ohms in neurons 500µ or greater in diameter. The surface of these neurons contains many membrane infoldings, such that the actual membrane surface area is at least ten times that of a smooth sphere of the same diameter. Using these values the specific membrane resistance (Rm) same diameter. Using these values the specific membrane resistance (R_m) has a minimal value of about 100,000 ohm cm². This is 100 times the value of R_m for squid giant axon. The very high membrane resistance provides an

explanation for many of the differences between the two preparations.

When Aplysia neurons are exposed to inhibitors of Na+ transport there is a dramatic depolarization, reflecting the contribution of an electrogenic Na⁺ pump to resting membrane potential. There is, however, no change in the membrane resistance. However, on exposure to metabolic inhibitors (NaCN, NaN3, dinitrophenol) there is a dramatic and reversible decrease in membrane resistance, frequently but not always accompanied by a hyperpolarization. The increase in conductance is primarily if not exclusively to K⁺. The metabolic process controlling membrane K⁺ permeability may act by regulation of the concentration of free Ca⁺⁺ either through activity of a Ca⁺⁺ pump and/or a control of calcium binding to intracellular sites.

AMILORIDE, FUROSEMIDE, AND SODIUM REABSORPTION IN PROXIMAL TUBULE IN RATS. G. Carrasquer, T.W. Wilczewski and A.K. Olson. Univ. of Lou. Sch. of Med., Louisville, Ky., U.S.A.

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Microperfusion experiments have been performed to test the effect of amiloride and furosemide on sodium reabsorption in the proximal tubule. Proximal tubules were perfused with rat Ringer's containing 3H-inulin and 22Na following the technique of Sonnenberg and Deetjen. Twenty-one tubules were perfused as control, 11 tubules were perfused under the influence of amiloride, and 18 tubules were perfused under the influence of furosemide. The log of the ratio (collected fluid)/(perfused fluid) was plotted vs. the length of the perfused tubule. The calculated slopes of the regression lines were 7.7 x 10^{-2} mm⁻¹, 8.5 x 10^{-2} mm⁻¹, and 0.5 x 10^{-2} mm⁻¹ for 3 H-inulin in the control, amiloride, and furosemide treated rats respectively; and $^{-2}$ 9.1 x 10^{-2} mm⁻¹, $^{-2}$ 1.3 x 10^{-2} mm⁻¹, and $^{-1}$ 9.1 x 10^{-2} mm⁻¹ for 22Na in control, amiloride, and furosemide conditions, respectively. The unidirectional permeability to 22Na was calculated taking into account the change in inulin concentration. The values were 60.8 X 10⁻⁴ mm/sec., 44.7 X 10⁻⁴ mm/sec., and 34.6 X 10⁻⁴ mm/sec. for control, amiloride, and furosemide, respectively. Amiloride affected the unidirectional control of the change in the control of the control of the change in the control of the change in th al permeability and not the net movement of salt, while furosemide affected both. A hypothetical model is to be tested further: Two passive pathways for Na, one functionally connected to and the other independent from the active pump. Amiloride might affect the independent pathway; while furosemide might affect the dependent passive component directly, the active pump directly, or both simultaneously. Supported by the USPHS.

LONG-LASTING HYPERPOLARIZATION OF CUTANEOUS PRIMARY AFFERENT TERMINALS. E.J.A. Carregal and B.L. Crue. Univ. So. Calif. Sch. Med., Los Angeles; and City of Hope, Duarte, Calif., 292 Post-tetanic potentiation (PTP) is easily demonstrable in spinal motor pathways but not in sensory pathways. It is thought that PTP is due to a long-lasting hyperpolarization of the U.S.A. presynaptic terminals produced by a tetanic burst in the parent fibers. We performed two types of experiments in an attempt to demonstrate hyperpolarization in the intraspinal terminals of cutaneous sensory fibers subjected to a tetanic burst. In one group of sodium pentobarbital anesthetized or decerebrate cats we tested the excitability of the intraspinal terminals of the sural nerve by Wall's technique before and after a tetanic burst to the sural nerve. The excitability of the intraspinal terminals was found to be decreased immediately following the tetanus and it did not recover for several minutes. In another group of experiments we recorded the dorsal root reflex (DRR) in the sural nerve following stimulation of the ipsilateral sciatic nerve, and we found the DRR to be absent for up to 30 secs. after the tetanus and recovering slowly within a few minutes. In both cases the sodium pentobarbital decreased the intensity of the phenomena considerably. These results indicate that repetitive activation of the primary afferents from the skin hyperpolarizes their presynaptic terminals and yet the postsynaptic discharge is not increased. This is interpreted by postulating that the presynaptic facilitation is accompanied by postsynaptic inhibition. In the absence of peripheral input it is tempting to postulate the existence of reverberating activity centrally.

VASODILATORS, INTRARENAL BLOOD FLOW AND NATRIURESIS IN DOGS. S. Carriere, J. Friborg and J.P. Guay. Department of Medicine, Maisonneuve Hospital and University of Montreal, CANADA.

In dogs anesthetised with pentobarbital the intrarenal infusion of prostaglandin (PGE1) 6 $\mu g/min$ and acetylcholine (Ach) 33 $\mu g/min$ produced a significant increase of the outer and inner cortical blood flow rate whereas the outer medullary blood flow rate remained constant. Silicone rubber injections and autoradiograms also suggested that the vasodilatation was generalized to the whole cortex as demonstrated by the Kr85 disappearance curves. The glomerular filtration rate remained constant and the mean diameter of the glomerular tufts of the outer as well as the juxtamedullary cortex were unchanged after vasodilators, findings which do not favor the hypothesis of an intrarenal redistribution of the glomerular filtration rate to account for the natriuresis observed in such conditions. It seems to be more readily explained by an imbalance of the peritubular physical forces reducing sodium reabsorption by the superficial and deep nephrons of the kidney. A marked decrease in Epah was also observed, which could not be explained by a relative increase in the medullary blood flow but possibly by the increased cortical blood flow rate.

294 ENERGY-INDEPENDENT BINDING OF CATIONS BY SARCOPLASMIC RETICULUM. Arselio P. Carvalho. Institute for Muscle Disease, New York, N.Y. 10021, USA.

The passive binding of Ca++, Sr++, Mg++ and the release of H+ by sarcoplasmic reticulum isolated from skeletal muscle of rabbit was examined before and after the reticulum was rendered lipid-free by treatment with acetone or after the action of phospholipases A and C or of trypsin. The results show that both the lipid and protein moieties bind cations passively. Furthermore, the phospholipases or trypsin, which release Ca++ accumulated actively in the presence of ATP, cause a marked increase in the passive binding of Mg^{++} . Passive binding of Ca^{++} , Sr^{++} , or Mg^{++} induces the release of H^+ . The maximal cation binding capacity of reticulum is about 300 neq/mg protein and the ratio of H^+ released to Ca^{++} bound is about 1.2 at pH of 7.0 or lower, but decreases markedly at higher pH values. The release of H+ and the binding of the cations is decreased by 40-50% when the reticulum is extracted with acetone. A competitive type of binding was observed for the various cations, except that Zn++ also interacts with sites not normally occupied by Ca++, Sr++ or Mg++. It is concluded that the action of the phospholipases or of trypsin on the reticulum increases the number of binding sites accessible to cations in the external medium in addition to rupturing the active transport mechanism for Ca++. The binding sites are present in the lipid and protein moieties which behave as cation exchangers. (Supported by a Grant from Muscular Dystrophy Association of America and by NATO Grant #388.)

SPINAL PRESYNAPTIC INTERACTIONS: LATENCY, FIBER COMPOSITION AND AFFERENT CONTROL OF THE DORSAL ROOT REFLEX IN BARBITURIZED CATS. K. L. Casey and B. Oakley. Depts. of Physiology and Zoology, Univ. of Mich., U.S.A.

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Using anodal polarization block and peripheral collision techniques it was determined that the afferent limb of the dorsal root reflex (DRR) in cutaneous nerves is mediated by the larger A fibers alone, the "efferent" limb by all sizes of A fibers including A-delta; whereas C fibers play no apparent role in the DRR. The dominant pattern of connectivity is large to small, i.e. large fibers elicit a DRR in smaller fibers. Consequently, electrical stimulation of a cutaneous nerve invariably results in reduced delta fiber input---- the outgoing DRR collides with the delta component of the incoming volley. It is unlikely that interneurons mediate all components of the DRR, since many intra-spinal latencies, measured by a novel collision technique, are less than 1.0ms. 10sec of natural skin stimulation or electrical stimulation of a nerve (100/sec) produce at least 30sec of DRR depression. Our findings indicate that this DRR depression is not solely attributable to effects restricted to the primary afferent terminals invaded by the orthodromic conditioning volley. Some DRR depression may result from large fiber activation of an interneuronal system in association with primary afferent depolarization.

AN ANALYSIS OF THE EFFECTS OF FENESTRAE ON THE PERMEABILITY OF BLOOD CAPILLARIES J. R. Casley-Smith. Dept. of Zoology, University of Adelaide, South Australia.

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Endothelial fenestrae are very frequent in some regions of the body, especially where large molecules are likely to occur in high concentrations - through manufacture, ingestion, poorly functioning lymphatics, or the excretion of volumes of water. Thus, a priori, it is possible that fenestrae may be concerned with the removal of macromolecules to the blood. This is strengthened by their antedating lymphatics phylogenetically, being permeable to large molecules, much more common on the venous limbs of capillaries (as necessitated by the flow of fluid-bearing proteins through the tissues) and by some evidence of molecular sieving. Measurements and counts on intestinal and adrenal cortical fenestrae (on venous limbs) have been used to calculate the inward and outward protein fluxes, due to convexion and diffusion, for various net hydrostatic and osmotic pressure differences. It is evident that there is a net uptake of macromolecules (once certain dimensions are exceeded) which increases till they are too big to pass through the venous fenestrae, i.e. there is effective 'directional permeability.' Similarly the outward flux through the far fewer arterial fenestrae can be calculated. It can be shown that, under most normal conditions, there will be local circulation of proteins resulting in their net removal, which is orders of magnitude greater than the outwards passage via vesicles and subsequent removal via lymphatics. Thus if fenestrae are present this local turn-over renders meaningless permeability measurements based on blood-lymph ratios.

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EXCHANGE DIFFUSION AND KINETIC EVIDENCE FOR A MOBILE CARRIER SYSTEM TRANSLOCATING CALCIUM ACROSS THE BRUSH BORDER MEMBRANE OF RAT DUODENUM. W. F. Caspary, Div. of Gastroenterology and Metabolism, Dept. of Medicine University of Göttingen, Germany.

Controversy exists whether calcium absorption by the small intestine is governed by a carrier-mediated entry-step or by a diffusional process. Entry of calcium into the epithelial cells was studied from the unidirectional influx of 45Ca into slices of everted rat duodenum. Uptake of 45Ca exhibited saturation kinetics with an apparent transport km of 0.9mM when studied over a 100-fold range of calcium concentrations. In order to test whether the rate-limiting step of uptake during the first minutes is a binding process within the cells rather than the transfer across the brush border membrane tissue was saturated with unlabelled calcium prior to the tracer experiments. Preincubation with unlabelled calcium considerably increased subsequent influx of 45Ca, but presence of unlabelled Ca in the incubating medium inhibited influx of labelled 45Ca. Demonstration of a saturating process for uptake and the phenomenon of exchange diffusion are strong arguments in favor of a mobile carrier and indicate that transport of calcium across the brush border membrane in rat duodenum is actually the rate-limiting step of initial uptake. (Supported by DFG).

RELATIONS BETWEEN CORTICAL DC SHIFTS AND MEMBRANE POTENTIAL CHANGES OF CORTICAL NEURONS ASSOCIATED WITH SEIZURE ACTIVITY.

H. Caspers, E.-J. Speckmann, R.W. Janzen. Inst. of Physiology, Univ., Münster(Westf.), German Fed.Rep.

The origin of DC shifts associated with seizure discharges and seizure inhibition in central nervous structures was studied by simultaneous recordings of the DC component and of the membrane potential of single neurons in the motor cortex of cats. The following results were obtained: 1) Increase of seizure susceptibility initiated by intravenous application of pentylenetetraxl is accompanied by a slow surface-negative DC displacement. This effect corresponds to a sustained depolarization of cortical neurons. With the appearance of EEG-spikes additional negative DC deflections are to be found. They coincide with paroxysmal depolarization shifts (PDS) in single units. 2) Seizure inhibition released by rising pCO₂ is usually associated with surface-positive DC deflections and with distinct hyperpolarization of cortical neurons. The findings suggest that cortical DC shifts occurring in various convulsive states are, primarily, neuronal in origin. They can be attributed to a summation of slow membrane potential changes in single elements.

LOCALIZATION OF CHANGES IN PULMONARY VASCULAR RESISTANCE IN RESPONSE TO CHANGES IN BLOOD GASES IN MATURE FETAL AND NEWBORN GOATS. S. Cassin, R. Gilbert, J. Hessler and D.V. Eitzman. Depts. of Physiology, Comp. Med., and Pediatrics, Univ. of Fla. Col. of Medicine, Gainesville, Fla. 32601

Experiments were carried out to localize the sites of change in pulmonary vascular resistance of fetal and newborn goats in response to changes in blood gases. Techniques used to calculate resistance have been described previously (Gilbert and Otis. Fed. Proc. 29:775, 1970; Cassin, Hessler & Eitzman. Fed. Proc. 29:776, 1970). The method is based on the assumption that there are Starling resistors in the pulmonary circulation; this allows the calculation of the resistance proximal to (Rp) and distal to (Rp) the Starling resistors. In all animals measurements were made on the lower lobe of the left lung. In fetal animals the left lung remained unventilated throughout the entire procedure and the right lung only was ventilated. In these animals neither Rp nor Rp in the left lower lobe changed when the right lung was ventilated with a gas mixture (4% $0_2 + 6$ % 0_2 in 0_2 which did not change blood gases. However, both Rp and Rp decreased significantly when the right lung was ventilated with air, which increased the 0_2 of the blood entering the left lower lobe. In newborn goats both Rp and Rp increased significantly when the gas ventilating both lungs was changed from air to 5% 0_2 in 0_2 . These data suggest that an increase in the 0_2 of the blood passing through the pulmonary vasculature results in a decrease in both Rp and Rp in fetal and newborn goats. (Supported by NIH Grant HE 0834-04)

300 THE SODIUM EXTRUSION IN SMOOTH MUSCLE CELLS OF THE GUINEA-PIG'S TAENIA COLI. R. Casteels. Lab. of Physiology, University of Leuven, Belgium.

The sodium efflux from taenia coli cells proceeds at a rather fast rate (0.239 min $^{-1})$ and this rate is not significantly affected by exposing the tissue to a Na-free or K-free solution. From this observation it could be concluded that sodium extrusion in taenia does not depend on the external K. Therefore the sodium extrusion of K-depleted tissues has been investigated. The Na-efflux of such K-depleted tissues proceeds very slowly but increases by adding 5.9 K. This increase is completely inhibited by adding 10 μM ouabain. A similar activation of the sodium extrusion can be obtained by adding Rb. Cs and Li do not seem to affect the rate of sodium efflux. It can therefore be concluded that also in smooth muscle the activity of the sodium pump depends on potassium in the external medium. The finding that K-free solution has no effect on the Na-efflux from normal smooth muscle cells at 35°C can be explained by the fact that sufficient K ions are leaking out from the intracellular compartment in the extracellular space to maintain an active sodium extrusion.

MECHANICAL POWER DEVELOPED BY THE CONTRACTILE COMPONENT OF A MUSCLE SHORTENING IMMEDIATELY AFTER STRETCHING AT A GIVEN SPEED OR AT A GIVEN LOAD. G.A. Cavagna and G.Citterio. Istituto di Fisiologia Umana, Università di Milano, Milano, Italia.

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When the shortening of a toad sartorius on a Levin-Wyman ergometer (given speed) follows immediately stretching, the positive work done by the 'contractile component' (total work - elastic energy released by the series elastic elements) can be greater than when shortening takes place, without previous stretching, from an isometric contraction. This result has been confirmed on frog gastrocnemius; in this muscle the elastic energy was measured from the force-extension relationship of the series elastic elements determined up to the force values attained during stretching by the isotonic quick-release technique. However when the muscle is attached to an isotonic lever (given load) the speed of shortening of the contractile component of gastrocnemius is the same whether the muscle was previously stretched or not. In conclusion: when shortening takes place immediately after stretching the 'contractile component' appears to be able to exert a greater average force at a given speed, but it is not capable of a greater speed at a given load. The choice of the independent variable (speed or load) determines therefore the power output of muscle.

THE POWER-VELOCITY RELATION IN SPRINT RUNNING. G.A. Cavagna, L. Komarek and S. Mazzoleni. Istituto di Fisiologia Umana, Università di Milano, Milano, Italia.

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According to the force-velocity relation of muscle the mechanical power developed during contraction depends on the speed of shortening. The power output of the muscles accelerating the body forward in sprint running may thus be affected by the progressively increasing speed of the run. In this study the positive and the negative work done at each step to accelerate and decelerate the body forward was measured, during the first five seconds from the start, utilizing a platform sensitive to the force impressed by the foot. In general the power developed at each step during the acceleration forward increases with the speed, reaching 3-4 HP at 9.5 m/sec. However between 5 and 7 m/sec the power decreases, to rise again when the negative work done at each step, which is low and rather constant up to 7 m/sec, increases sharply with increasing speed. These results suggest that at low speed the contractile component of muscles is mainly responsible for the power output, whereas at high speed of run (7 to 9.5 m/sec) another component is added, i.e. the mechanical energy stored in the series elastic elements during stretching the contracted muscles (negative work) and released immediately after in the positive work phase.

AGING OF THE ERYTHRUCYTE. L. C. CERNY and F. B. COOK. Masonic Med. Res. Lab., Utica, N.Y. U.S.A.

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The life of the erythrocyte is approximately 100 days. During this period of time, it has been shown that the mean corpuscular volume and the mean hemoglobin concentration changes with age. It is possible to separate erythrocytes of different ages with density gradient techniques. In the present study, aged erythrocytes are examined both in terms of their life span as well as the age of the animal from which they were taken. By means of rheoscopy and capillary-pressure techniques, it is possible to examine the aging red cell membrane in terms of its elasticity, viscosity and interactions with the suspending fluid.

CHEMICAL IDENTIFICATION OF THE FENN EFFECT IN THE FROG GASTROCNEMIUS MUSCLE. P.Cerretelli and G. Ambrosoli. Inst. of Physiology, University of Milano, Italy. 304 The release of chemical energy (splitting of ATP and PC and production of lactic acid, L.A.) by the frog gastrocnemius during repeated tetanic contractions of dif ferent duration has been measured both in isotonic (load=600 g/g of muscle) and isometric (tension= 600 g/g of muscle) conditions. In both cases the energy consumption increases linearly with the duration of the tetanus and the cost of the tension main tainance is about 0.45 µMoles/g of muscle and per sec. The chemical energy involved in the activation process, including that required for both internal and external work performed by the muscle, as indicated by the origin of the two lines on the ordinates, amounts to 1.2 µMoles/g for the isotonic and 0.54 µMoles/g for the isomet ric. The difference between these values, i.e. 1.2 - 0.54 = 0.66 μ Moles/g may be interpreted as the chemical counterpart of the Fenn effect: as the work performed by the muscle contracting isotonically amounts to 201 gcm/g, the mechanical energy per mole of high energy phosphates split can be calculated as 3050 kgm or 7200 calories. Assuming that the efficiency of the transformation of the chemical into mechanical energy is about 0.65, the free energy change of one Mole of high energy phosphates involved amounts to 7200/0.65 = 11,000 calories.

ROLE OF THE OSMOLALITY IN THE REGULATION OF GASTRIC BLOOD FLOW. J. Chacin, 305 J.Colina and P.Díaz. Dept.of Physiology, Sch.of Med., Univ.of Zulia, Mara-

caibo, Venezuela. In anesthetized dogs with a semi-isolated preparation of the corpus of mach, the effects of the hyperosmolality on the resting mucosal blood flow (MBF) were studied. The i.v. infusion of hypertonic solution of glucoflow (MBF) were studied. The i.v. infusion of hypertonic solution of glucose or urea produced in arterial blood a significant increase of the osmolality and a decrease of the hematocrit and Na⁺. The plasma osmolality increased from 301.8+2.0 mOsm/kg (mean+S.E., N=16) to 342.2+8.1 (N=8). The MBF varied in parallel fashion with changes in osmolality, increasing from 1.47+0.12 ml/g/20 min (N=24) to 2.31+0.3 (N=8). The i.v. infusion of isotonic solution did not produce significant changes in the plasma osmolality and MBF. The intragastric instillation of hyperosmotic solution also produced a significant increase in the plasma osmolality of gastric venous blood and in The intragastric instillation of hyperosmotic solution also produced a significant increase in the plasma osmolality of gastric venous blood and in the MBF. The osmolality increased from 293.3+1.4 (N=17) to 302+2.2 (N=8), and the MBF from 1.06 ± 0.08 (N=31) to $1.68\pm0.\overline{21}$ (N=16). The total gastric blood flow measured by Fick principle also increased. The arterial pCO2, and Na+, K+ and hematocrit in arterial and gastric venous blood did not change significantly. It may be concluded that the hyperosmolality produces an increase of the gastric MBF, by which it is possible that this factor contributes to the increase of the MBF observed during stimulation of the gastric secretion.

BIOMOLECULAR TRANSFORM OF MONOTONOUS RHYTHMIC ACTIVITIES INTO BURSTING ENDOGENOUS ACTIVITIES IN PACEMAKER NEURONS (APLYSIA AND 306 HELIX). N. Chalazonitis . Inst. of Neurophysiology, C.N.R.S., Marseilles, FRANCE.

Molecules of respiratory and/or metabolic interest such as oxygen, hydrogen ions, etc.., can, at critical concentrations transform monotonous activities of regular frequency in identified pace maker neurons (Aplysia or Helix) to "bursting" or "waving" activities (1,2,3). The process is not of synaptic origin. Similarly, molecules of pharmacological interest: epileptogenic such as metrazol or cardiazol; anticonvulsant such as phenobarbital can determine analogous transformations (4). Antibiotics, such as cycloheximide, can even (apart from any inhibitory action on protein synthesis) transform neurons of stable membrane potential into waving neurons, through a simple pharmacological action (5).

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PARTICIPATION OF CENTRAL NORADRENERGIC NEURONS IN BARORECEPTOR REFLEXES.

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Disappearance rates of ³H-norepinephrine (³H-NE) given intracisternally and activities of tyrosine hydroxylase were examined in 5 brain regions (telencephalon, hypothalamus, midbrain, medulla-pons, and cerebellum) and in spinal cord regions (cervical, thoracolumbar, and lumbosacral) of rabbits acric nerves. Norepinephrine and dopamine levels in these CNS regions were not altered by denervation. ³H-NE turnover and tyrosine hydroxylase acticord (T₁ to L₃), the cord region containing the lateral columns that receive It seems likely that these changes reflect increased activity of noradrenerial baroreceptors and that they mediate the rise in blood pressure and/or heart rate that follows sino-aortic denervation. ³H-NE turnover also increased in the hypothalamus of denervated animals. (*Overseas Research Fellow, National Heart Foundation of Australia.)

THE ENDPLATE POTENTIALS IN THE EARTHWORM(PHERETIMA HAWAYANA)NEUROMUSCULAR PREPARATION. Y.C.. CHANG. Fisiologia, Universidade Federal do Paraná,

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Endplate potentials, EPPs, could be evoked from both levels of muscle membrane resting potential, E_m, of Pheretima hawayana by nerve cord stimulation. That from the first level(32 - 0.7 mV) was either an inhibitory endplate potential(IEPP) or an excitatory endplate potential (EEPP) superimposed with an IEPP. That from the second level(59.7-1.3 mV) was always an EEPP. Graded response(but never an all-or-none action potential with overshoot) could be evoked by summation of two second level EEPPs at certain intervals(firing level 10 mV). The amplitude of IEPP could be increased by (GABA) and that of EEPP of the second level could be increased by either (GABA) or (Na-glutamate) until graded response was evoked by a single stimulus. Curare suppressed the EEPP of the second level and prostigmine enhanced it without affecting the EPPs of the first level. No change in E or its spontaneous discharge was observed either during electrical stimulation or after drug treatment. It was thus postulated that the E-junctions in the second level might be cholinergic and the I-junctions(or interneurons) in the first level of the GABA-type while the glutamate E-junction might present in both levels. (Supported by Cons. Nac. Pesq. Grant No. 8475/67 and CAPES Grant No. 16.447/67).

THE EFFECTS OF PROSTAGLANDIN E1 ON O2 CONSUMPTION IN COLD-ADAPTED RATS. C.F.K. Cheng and J.C.C. Wang, Dept. of Physiology, Univ. of Hong Kong, Hong Kong.

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Prostaglandin E₁ (FGE₁) inhibits norepinephrine (NE)-induced lipolysis (Steinberg et al., Biochem. Pharmacol. 12:764, 1963) and NE increases O₂ consumption (CC) in cold-adapted rats (Ksieh and Carlson, Am. J. Physiol. 190:243, 1957). The effects of FGE₁ on OC are studied in anaesthetised, curarised cold-adapted rats with the following findings: (1) intravenous infusion of FGE₁ at 25 µg/ml/hr decreases OC, with an initial rapid decline to 40-65% of the preinjection value in 2½ to 4 minutes, followed by partial recovery to 85 to 90% within 5 to 10 minutes which is then maintained until the end of infusion; (2) intravenous injections of FGE₁ inhibit the increase in OC induced by continuous NE infusion; (3) intravenous injections of NE inhibit the decrease in OC induced by continuous FGE₁ infusion; (4) simultaneous infusions of FGE₁ (25 µg/ml/hr) and NE (33 µg/ml/hr) produce only slight changes in OC. In control rats, FGE₁ infusion gradually decreases OC to 80-90% without the phasic changes observed in cold-adapted rats, and FGE₁ and NE have the same antagonistic relationship as in cold-adapted rats. It is proposed that the effect of FGE₁ and NE on OC are probably mediated via the same mechanism as their lipolytic effects, viz., via the cyclic adenosine-monophosphate system which is at a higher level of activity in cold-adapted rats.

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ACCT OF EMHILIC ALCOHOL ON HEPATO-CARDIOVASCULAR DYSTROPHIES INDUCED BY APHEROGENIC DIEF. G.Chera, D.Dolinescu, G.Volcinschi, M.Wihailä, C. Haller, I.Mitulescu. Institute of Public Health and Medical Research, Academy of Medical Sciences, Jassy, ROMANIA.

Adult rats on normal or atherogenic (40% casein, 31% starch, 21% sunflower oil, 3% cholestarol, 0.3% methylthiouracil, 1 % cholic acid) diets were given orally 1 ml/loo g body weight of a 15% alcohol solution, duwere given orally 1 ml/loo g body weight of a 15% alcohol solution, during 50 days. Some animals were also given i.m. 40.000 IU/loo g Vit.D on ring 50 days. In rats fed a normal diet biochemical and morphological the first 4 days. In rats fed a normal diet biochemical and morphological exams showed that alcohol induced steatosis and various liver cytoplasmic dystrophies, without significant variations in cholesterolemia and total dystrophies, without significant variations in cholesterolemia and total lipidemia and no cardiovascular morphological changes. In rats fed an alipidemia caused by the diet itself, aggravating steatosis and liver dystromia caused by the diet itself, aggravating steatosis and liver dystromial cuaing lipidosis of myocardial fibers. Under these conditions alcohol caused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological picture of aorta and corocaused significant changes in the morphological changes.

THE TRANSIENT VENTILATORY RESPONSE TO HYPOXIA AND HYPERCAPNIA. N.S. Cherniack, T.J. Trueb, N.H. Edelman, S. Lahiri and A.P. Fishman. Cardiovascular-Pulmonary Division, University of

Pennsylvania, Philadelphia, Pa., USA. The dynamic characteristics of the transient ventilatory response to hypoxia and hypercapnia become particularly important when environmental conditions are abruptly changed. In the present study a mathematical model of the ventilatory control system, which takes into account the role of body gas stores and regional circulation, was used to relate the location of CO2 receptors and of O2-CO2 interaction to the transient response to hypoxia and CO2. The model was based on experimental measurements of ventilatory responses as well as measurements of the effects of changes in ventilation on CO2 and O2 stores and upon cerebral blood flow. Analysis using the model showed: 1) an exclusively arterial CO2 and O2 receptor would respond rapidly, but unstably, to hypoxia alone or in combination with CO2; 2) an exclusively central CO2 receptor would respond slowly to CO2 and hypoxia and its response time would be slower the greater the responsiveness of cerebral blood flow to hypoxia and CO2; and 3) if hypoxic drive interacted entirely with arterial PCO2, instability of ventilatory responses would be greater than if interaction was with central PCO2. Rapid (but stable) responses to both hypoxia and CO2 occurred when 70% of the CO2 drive as well as all the $\rm CO_2$ - $\rm O_2$ interaction was considered to occur at a central site, in accord with our experimental findings in awake man. This agreement suggests that $\rm CO_2$ receptor sites and 02-CO2 interaction are optimally located to ensure that the steady state is achieved smoothly and rapidly, so that the organism suffers minimal derangement of gas tensions during transient states of hypoxemia and hypercapnia.

312 INITIATION OF RESPIRATION OF THE FETUS BY DIRECT ELECTRICAL STIMULATION OF THE BRAIN STEM: V. Chernick, A. Sklenovsky, V. Haylicek and R.D. Pagtakhan. Depts. of Physiology & Pediatrics, Univ. of Manitoba, & Children's Hospital, Winnipeg, Canada.

The mechanisms which ensure fetal apnea and the initiation of respiration at birth are poorly understood. Direct study of the fetal respiratory center has not been previously undertaken. We have mapped the inspiratory center of the exteriorized fetal sheep near term using sterotaxic placement of a stimulating electrode in the region of the medulla. Ventilatory efforts were monitored by connecting the trachea to a liquid plethysmograph. The results were compared to similar mapping of the respiratory center of the newborn lamb. The fetal respiratory center was quite diffuse, extending from the obex to the lower pons and 2.5 mm on either side of the midline. In contrast, the respiratory center of the newborn lamb was more localized, extending only 6 mm rostral to the obex. In the unanesthetized fetus the threshold current required to initiate respiration was 0.15 ± .06 ma. Stimulation of a similar area in the unanesthetized newborn lamb caused appear at 0.33 ma. It is concluded that the respiratory center is not actively inhibited during the latter portion of gestation and therefore cannot account for respiratory inactivity in utero.

Supported by the Medical Research Council of Canada and the Research Fund, Children's Hospital.

PERMEABILITY OF WALLS OF THE MICROVASCULAR BED ON CELLULAR AND SUBCELLULAR LEVEL. A.M.Chernukh. Inst. of Normal and Pathological Physiology AMS, Moscow, USSR.

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Combination of biomicroscopical, biochemical methods and electron microscopy has been used. Particular features of permeability of histo-hematic barriers as well as those of membranes of cellular organelles under the influence of vasoactive substances, X-ray irradiation, neuro-bances of membrane permeability under the action of drugs with P-vitamin activity (esculamine a.others) have been shown. It has been established that changes in intensity of the microvascular process and the formation of microvesicles of capillary endothelium represent an adaptation reaction on ultrastructural level.

ACTION OF VASOPRESSIN ON THE FUNCTIONAL STATE OF HYPOTHALAMUS AND CEREBRAL CORTEX. A.M.Chernukh and M.D.Vakar. Inst. of Normal and Pathological Physiology AMS, Moscow, USSR.

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In chronic experiment (on unanesthetized animals) the functional state of hypothalamus and cerebral cortex has been studied on the base of data of their bioelectrical activity (synchronous registration with electrocardiogram and respiration) with subsequent intracerebral, intravenous and intramuscular injection of vasopressin, POR₈1) (fom 0,1 to 5 units per 1 kg of body wieght). Differences in reactions depending on the method of applying the drug have been established. It has been demonstrated that the effect of vasopressin is obtained as a result of direct action on hypothalamic centres as well as through the sympatho-adrenal system.

1) The authors wish to express their gratitude to the firm "Sandoz" (Switzerland) for kindly placing vasopressin, POR8 at our disposal.

MODEL OF DYNAMIC RESPONSE OF HEART PERIOD TO LARGE CHANGES IN RATE OF VAGAL STIMULATION IN THE CAT. G.F. Chess and F.R. Calaresu, Faculty of Engineering Science and Department of Physiology, The University of Western Ontario, London, Canada.

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A model of the dynamic relation between changes in heart period and small variations in rate of stimulation of either vagus in chloralosed vagotomized cats pretreated with propranolol has been obtained previously using frequency response methods (Chess and Calaresu, Am.J.Physiol., in press). To obtain a more comprehensive model this study has been extended by applying step functions in the rate of stimulation (range 8 - 50 Hz) of either vagus in similarly prepared animals and using time domain methods of analysis. The strengths of the stimuli were such that a sinus rhythm was maintained as could be judged by monitoring the electrocardiogram. A typical response to a step function was an increase in heart period to a new steady value preceded by an "overshoot" and followed, after the stimulus was removed, by "postvagal tachycardia". It is unlikely that the overshoot and tachycardia were due to stimulation of sympathetic fibres in the vagus as the sympathetic system was blocked by propranolol. The observed dynamic behaviour may be described by a model consisting of a third-order system with variable coefficients and an intrinsic negative feedback. It is suggested that the overshoot and tachycardia may be causally related to mechanisms such as changes in the availability of neurotransmitter during stimulation and/or stretch of nodal tissue. (Supported by the Ontario Heart Foundation.)

MESURE DU DEVERSEMENT DE CHOLESTEROL DANS LE TUBE DIGESTIF DU RAT. F. Chevallier et Cl. Lutton. Lab. de Physiologie de la Mutrition, Faculté des Sciences - Orsay, France. 316

Des rats adultes ingérant un régime contenant 0,013 p. cent de cholestérol-4-14 c sont sacrifiés à 7 différents temps d'un nycthémère. Pour chaque période intercalaire on note la quantité de nourriture ingérée, les nombres de crottes intrastomacales et recueillies dans la cage. La coprophagie atteint 45 p. cent des crottes émises. On étudie, par ailleurs, la radioactivité et la composition en stérols (chromatographie en phase gazeuse) des contenus de l'estonac, de l'intestin fragmenté en 4, du caecum, du colon et des excréments.
L'ensemble des résultats permet I) de définir l'apport alimentaire et excrémentiel en cholestérol, coprostérol et divers autres stérols, 2) de calculer par dilution isotopique cnolesterol, coprosterol et divers autres sterols, 2, de taleure par diversif. Dans l'esto-le flux de cholestérol endogène déversé dans chaque segment du tube digestif. Dans l'esto-mac, le flux de cholestérol endogène vient doubler l'apport alimentaire en cholestérol. L'intestin est le siège d'un réel cycle entéroplasmatique dont la vitesse est précisée. Dans le caecum et le colon, il n'y a ni absorption ni déversement. Les résultats sont discutés en rapport avec les origines des stérols fécaux.

EFFECT OF YOGIC PRACTICES ON SOME BODY FUNCTIONS. G.S. Chhina, Dept. of Physiology, All India Inst. of Medical Sciences, New Delhi-16, INDIA. 317

Yogis claim to develop voluntary control over their body functions.

The modification of metabolic activity, body temperature, muscle tone
and some central nervous mechanisms by yogic practices has been verified.

The physical price for these achievements of yogis appear to be The physiological basis for these achievements of Yogis appear to be predominantly related to conditioning and learning of visceral responses. Although control over cardiac and smooth muscle activity has also been observed some of these effects are related to indirect result of striated muscle activity. The data relating to these observations will be discussed.

A NEW SINGLE BREATH OXYGEN DILUTION METHOD FOR FRC DETERMINATION. S.T. Chiang and R. Yang. Dept.of Med., National Defense Med.Center and Taiwan Vet. Gen.Hosp., Taipei, Taiwan, Republic of Chian.

A new oxygen dilution method for measuring functional residual capacity 318

(FRC) has been devised. In principle it is open circuit and single breath plus 15"breath holding. The method is very simple and substantially reduces the

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Twenty-two normal subjects were studied by this method. For comparison, the conventional 7 minute nitrogen washout method and 7 minute helium equilibrium method were performed in the same group. Mean values for FRCs are not significantly different (p > 0.1)among these 3 techniques and similar to those reported in literature for normal subjects(FRC=3.021 L±S.D.0.569 with subject mean age:27.5 years old and mean height:167 cm). The advantages of this method are:(1)the equipment is simple;(2)the result is rapidly available:(3)capable to measure FRC during exercise and at other special conditions Therefore, it makes population study of FRC and FRC study at special conditions possible. The disadvantage is that it cannot be applied to the patients with marked uneven ventilation.

EFFECT OF pl. ON THE LIPOLYSIS INDUCED BY EPINEPHRINE. G.E.Chiappe de Cingolani and F.V.Vega. Inst.of Physiology. Sch.of Med.of La Plata. Argentina.

The inhibition of lipolysis induced by epinephrine during acidosis has been previously described. However, data were not reported with regards to the effect during alkalosis.

The present study was carried out with isolated fat cells from rat epididymal fat pad incubated for 1 h at 37°C. Lipolysis was determined measuring free fatty acids and glycerol released to the incubation medium. The fat cells were incubated in the presence of epinephrine at pl! 6.8; 7.4 and 7.8. The different pls were obtained by changing sodium-bicarbonate concentration at a pCO₂ of 40 mm of lg. The results obtained showed a maximal lipolytic response at pl! 7.4 (P < 0.01). To study through which mechanism acidosis or alkalosis inhibit the lipolysis induced by epinephrine, a second serie of experiments was done in the presence of cyclic-3'5' APP. The results obtained also showed a higher lipolysis at pl! 7.4, being inhibited at pl! 6.8 and 7.8 (P < 0.01). It is concluded that either acidosis or alkalosis inhibit the lipolysis induced by epinephrine. The same results are obtained when cyclic-3'5' AMP is used as a lipolytic agent. Finally it is suggested that the inhibition by acidosis and alkalosis of the lipolysis induced by epinephrine vould occur in some step after the formation of cyclic-3'5' AMP.

EFFECTS OF Mn++ ON THE MECHANICAL PROPERTIES OF FROG SINGLE MUSCLE FIBERS. D.J. Chiarandini and E. Stefani. Inst. Gen. Anat. Fac. of Medicine, Buenos Aires, Argentina.

The effect of Mn (5-20mM) on twitch, potassium and caffeine contractures was studied in single muscle fibers of the frog Leptodactylus ocellatus. Simultaneous recordings of tension and extracellular spike showed that 10mM Mn reduced within 10 sec. the twitch amplitude to 25% of the control value and that the spike was somewhat prolonged and appeared with a longer delay from the stimulus artifact. The intracellularly recorded spikes showed no changes in the overshoot while the afterpotential was prolonged and begun at a more positive membrane potential. K-induced contractures (KxCl constant) were also depressed or abolished. In the presence of 10mM Mn the threshold K concentration, (K) $_{\rm O}$, for eliciting tension shifted from 20mM (-48mV) in controls to ca. 35mM (-33mV). Dose-responses curves showed a parallel shift towards higher (K) $_{\rm O}$. Caffeine (4mM) contractures were unaffected by Mn. The blocking effect of Mn on the twitch and K-contracture could be explained by the observed change in the mechanical threshold. This effect may be related to the well established property of Mn of blocking the permeability to Ca in other systems, and it could be thought that a Ca traslocation across the mechanical response.

CIRCULATORY AND METABOLIC CHANGES IN HEMORRHAGIC SHOCK IN THE MONKEY. Shu Chien, Shunichi Usami, Robert J. Dellenback, Anthony M. Benis and Kung-Ming Jan. Lab. of Hemorheology, Dept. of Physiology, College of Physicians and Surgeons, Columbia Univ., New York, N. Y. 10032, U. S. A.

Circulatory and metabolic changes in hemorrhagic shock were studied in stumptail monkeys (Macaca Speciosa) without general anesthesia. Arterial pressure was maintained at 40 mmHg for three hours, and measurements were made in the control period, during oligemia and following retransfusion. Measurements included blood volume (albumin-Il25 and RBC-Cr51), cardiac output (dye dilution), hematocrit, plasma protein concentration, blood pO2, pCO2 and pH, and blood concentrations of pyruvate, lactate, glucose and uric acid. In comparison to the dog, less bleeding was needed in the monkey to reduce the arterial pressure and cardiac output to given levels. Monkeys showed anaerobic metabolism and metabolic acidosis during oligemia, but respiratory compensation was less effective than in dogs. The intensity of metabolic disturbance can be correlated with the severity of circulatory disturbance during oligemia, but not following retransfusion. (Supported by U.S.P.H.S. Research Grant HE-06139, U.S. Army Contract DA-49-193-MD-2272, and Gifts from the Scaife Family in Pittsburgh).

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322 NET SYNTHESIS OF ATP BY REVERSAL OF THE Na-K-PUMP IN RABBIT NON-MYELINATED NERVE FIBRES.

M. Chmouliovsky-Moghissi and R.W. Straub, Inst. of Pharmacology, Univ. of Geneva,
Switzerland.

Synthesis of ATP by reversal of the Na-K-pump has been demonstrated in erythrocytes ghosts and intact red cells e.g. (Glynn and Lew, J. Physiol. 207, 393, 1970). In the present experiments similar conditions were realized for non-myelinated nerve fibres. Desheathed rabbit vagus nerves were first incubated for 45 min in Na-free K-rich Locke containing 4 mM iodoacetic acid. At the end of this period the ATP level determined by containing 4 mM iodoacetic methods, fell from 1,8 mM/kg wet nerve to a mean of 0,12 mM. The nerves were then divided into two groups: group A was transferred to K-free Locke containing iodoacetic acid, group B to a similar solution with, in addition 0,13 mM ouabain. After 15 min the Na, K and ATP contents were measured; further, in some preparations it was shown by electronmicroscopic examination, that the fibre membranes were intact. The ATP content of group A amounted to 171 ± 41% (n = 19) of that of group B, suggesting that net synthesis of ATP may occur in these conditions by reversal of the Na-K-pump.

Supported by FNRS grants No 4540, 3.286.69 and C.F. Boehringer GmbH.

233 EFFECTS OF ACUTE AND REPEATED EXPOSURE TO COLD ENVIRONMENT ON BODY TEMPE-RATURE AND PLASMA 17-OHCS IN INTACT AND DEAFFERENTATED RATS. I. Chowers, N. Conforti and S. Feldman. Lab. of Exper. Endocrinology, Dept. Med. 'A' and Dept. Neurology, Hadassah University Hospital, Jerusalem, Israel.

Male rats were exposed to 0°C for 30' for 3 times. They were divided into control (C); rats with complete hypothalamic (hypoth.) deafferentation (deaf.) (CHD); rats with anterior hypoth. deaf. with small (AHDS) and large cuts (AHDL) and posterolateral hypoth. deaf. (PLHD). Plasma 17-OHCS after the first exposure was 33.9±2(C), 18.9±1.7 (CHD), 32.6±2.3 (AHDS),10.8±2.2(AHDL) and 19.4±2.8 (PLHD) µg/100 ml, respectively. On third exposure only in the control group a difference was found (27.4±1.6 µg/100 ml), p<0.02 when compared to first exposure. Maximal drop in rectal temperature (RT) was -4.2°C and minimal -1.7°C. The following degrees in drop of RT were observed on the first exposure; CHD>AHDS>AHDL>PLHD>C, while following the third exposure the order was PLHD>C,AHDI>CHD>AHDS. Results indicate a) that on cold exposure, ACTH secretion is partially modulated by thermosensitive elements b) the interconnection between the anterohypothalamus and median eminence enable the animals to preserve better its body temperature. However these interconnections may be compensated by other neural pathways.

ANALOGS OF BASIC AMINO ACIDS AND CITRULLINE IN RENAL TUBULAR TRANSPORT. H. N. Christensen and A. M. Cullen. Dept. of Biol. Chem., Univ. of Mich., Ann Arbor, Mich., 48104 U.S.A.

To study some rather mystifying interactions between basic and neutral amino acids (including particularly cystine) for renal tubular transport, we have synthesized a series of non-metabolizable analogs of the structures,

and R-N When R or R' was the guanyl group, and NH3 NH3. the amino acids therefore arginine analogs, their biological half-lives in the rat were 10 and 6 days, respectively, and nearly complete tubular resorption was evident. Intraperitoneal injection of 5 mmoles/kg body weight of homoarginine or its piperidine analog, R=guanyl, greatly intensified the renal losses of all basic amino acids plus cystine and citrulline. But if R' was H, citrulline excretion rose without significant increases in cystine or arginine. If R' was guanyl, citrulline excretion was increased 100-fold, lysine loss 50-fold, with only minor effects on cystine and ornithine. Renal citrullinuria could be stimulated in the absence of lysinuria, whereas cystinuria was not. Conversely, injection of α -aminoisobutyric acid stimulated lysinuria and cystinuria but not citrullinuria. The citrulline analog, R=carbamyl, stimulated large losses of cystine and basic amino acids. The unequivocally neutral citrulline thus appears to join cystine in its known association with the basic amino acids, raising new doubt of the adequacy of Dent's hypothesis that the second -NH¹/₃ group of cystine underlies that association. (Assisted by Grant HD-01233, N.I.H., United States P.H.S.)

CONTROL OF DENTAL PULPAL PRESSURES AND RELATED OBSERVATIONS ON MANDIBULAR CIRCULATION AND MARROW PRESSURES. R.L.Christiansen, M.W.Meyer and M.B.Visscher. Dept. of Physiology, Univ. of Minnesota, Minneapolis, Minn., and Natl.Inst. of Dental Res., Bethesda, Md. USA.

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A study was conducted on 32 young dogs to develop a more reliable system to measure dental pulpal pressures and explore these pressures under conditions of controlled perfusion flow changes. The right mandibular artery and vein were isolated and cannulated to perfuse the right mandible and to measure the venous end-pressure of the perfused vascular bed. A micromanipulator-controlled cutting instrument was used to expose the dental pulpa and the mandibular marrow. Miniature pressure transducers were utilized to determine the tonometric pressure plateau of the pulpal and the marrow tissues. Conventional closed cannulation was performed on another tooth to serve as a comparison for the new tonometric method of pulpal pressure measurement. The pressures were studied under conditions of autoperfusion and step flow controlled perfusion. The tonometric dental pulpal and mannespectively. The venous end-pressure was 16 \pm 8 mmHg at a mean perfusion pressure of 156 \pm 28 mmHg. The tonometric pulpal pressures were lower and were less variable than the investigators. The correlation coefficient between the tonometric pulpal pressure and venous pressure was 0.85 over a large range of arterial and venous pressures. The cannulation procedure yielded a much lower correlation with the venous pressure (r = 0.47).

A SMOOTH MUSCLE-ACTING FACTOR [SMAF] EXTRACTED FROM LUNG. <u>C. Chryssanthou</u>, <u>F. Teichner</u>, <u>G. Goldstein</u> and <u>W. Antopol</u>. Mount Sinai School of Medicine of the City University of New York, and Beth Israel Medical Center, New York, New York 10003, U.S.A.

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A smooth muscle-acting factor [SMAF] has been found in human, rabbit and mouse lung. SMAF is extracted in 1N HCl and partially purified by solvents, dialysis and column chromatography. The preparation is dialyzable, water and alcohol soluble, ether insoluble, heat stable and homogeneous on Sephadex G-25, thin layer chromatography [TLC] and high voltage electrophoresis. It is ninhydrin positive and gives negative reactions with reagents for carbohydrates and lipids. Incubation of the preparation with aminopeptidase or carboxypeptidase B results in at least one additional spot on TLC. SMAF exhibits the following pharmacological actions: [1] Elicits slow weak contractions of the isolated guinea pig ileum and rat uterus. [2] Produces bronchoconstriction in the guinea pig. [3] Exhibits hypotensive effect [rat]. [4] Increases capillary permeability ["blueing" of the rabbit's skin]. [5] Potentiates effects of acetylcholline, histamine and particularly bradykinin on isolated organs and on intact animals. The ability to increase responsiveness of smooth muscle to stimulants is one of the most striking properties of SMAF. Physicochemical and pharmacological properties of SMAF differentiate it from similar substances. SMAF, a hitherto unknown humoral factor, probably a polypeptide[s], may play important pathophysiological roles by modifying the capacity of smooth muscle cells to respond to stimuli. [Aided by Contract NO0014-68-A-0393 [NR 101-735] of the Office of Naval Research, Department of the U.S. Navy and the Saul Singer Foundation].

RHEOLOGICAL PROPERTIES OF LIVING TISSUE. Billie Mae Chu, Wallace G. Frasher and Harold Wayland, Div. of Engr. and Applied Sci., California Institute of Technology, Pasadena, California 91109, U.S.A.

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The hysteretic behavior of living tissue (cat's mesentery) in strip biaxial deformations has been measured and concomitant observations on structural changes and recovery have been made to determine the extent to which the latter can be used to explain the hysteresis. It has been observed that the tissue continuously degrades, i. e. suffers a decrease in modulus, if the gross sequence of loading cycles is continuous. However, if a period of recovery time of about five minutes is permitted between the overall loading cycles, the tissue will either completely or partially recover. A hysteresis model based on a microfailure criterion is proposed and is correlated with photomicrographs of the tissue.

328 PEFFECT OF GLUCAGON UPON MYOCARDIAL POTASSIUM PALANCE. F.E. Cingolani, J.C. Marsiglia and E.A. Marincevic. Inst. de Fisiología, Facultad de Ciencias Médicas, La Plata, Argentina.

Negative myocardial K balance follows different positive inotropic interventions. Despite its myocardial positive inotropic effect, catecholamines present the opposite action. Such positive balance seems to be related to β -adrenergic receptors (Cingolani et al., Arch.int. Pharmacodyn. 176: 21, 1968). Since glucagon has similar cardiac actions to those of catecholamines, it was considered of interest to evaluate its effects upon myocardial K balance. Experiments were undertaken in an isolated and perfused dog heart preparation, similar to that of Heymans and Kochmann. In order to calculate myocardial K balance, coronary blood flow and arterial venous plasma K concentration were measured. Myocardial contractility was assessed by an isometric force transducer, sewn to the left ventricle wall. This signal was electronically differenciated in order to obtain df/dt. Feart rate was kept constant by right atrial pacing with electronic stimulation. Coronary administration of 100 up of glucagon was followed by a positive K balance of 59 ± 13 uEq/100g of heart muscle (P<0.01). This positive K balance was evident through approximately 10 min. This data tend to substanciate that glucagon has a similar β -adrenergic agonist action, on what myocardial K balance concerns.

329 PHYSIOLOGICAL AND PSYCHOLOGICAL FACTORS IN THE LONG-TERM CONTROL OF THE ENERGY BALANCE IN MAN. L.A.Cioffi and A.Speranza. Inst. of Human Physiology and Inst. of Psychology, Univ. of Naples, 80138 Napoli, Italy.

The components of the long-term control system of the energy balance in man have been studied in a research on the relationship between the obesity and some physiological and psychological factors. The evaluation of biological and nutritional parameters, and the analysis of some personality traits and of the psychological dynamics underlying individual food habits demonstrate that a peculiar biological constitution and a poorly structured and differentiated personality, when associated, induce a stable attitude toward food that is not connected anymore with the energy balance control. Furthermore, the final characteristics of this error of control are strictly related to the time of the onset, the duration, and the intensity of individual and environmental determinants.

330 CEREBROSPINAL FLUID, BLOOD, AND ASCITES-CATECHOLAMINES IN HEPATIC CIRRHOSIS. Al.Ciplea, G.Bubuianu, E.Bubuianu. D.Danielopolu Inst. of Normal and Pathological Physiology, Bucharest, Romania.

The consideration of the extensive inervation of liver parenchyma, together with data relating to the degradation of catecholamines in the liver and the importance of hepatic vascular process in hepatic cirrhosis, prompted us to investigate the behavior of catecholamines in this condition. The following parameters were measured in cerebrospinal fluid, blood and ascites fluid: catecholamines, epinephrine, and norepinephrine. During hepatic cirrhosis, total catecholamines level in blood, as well as in cerebrospinal fluid was reduced. This reduction could be attributed primarily to a decrease in norepinephrine. Since epinephrine remained almost normal, the fraction of epinephrine contributing to total catecholamines increased close to 0.5, which is higher than normal. Changes parallel to those found in the blood could be observed also in the ascites fluid.

SUBSTANCE P, A POSSIBLE TRANSMITTER SUBSTANCE OF THE MYENTERIC NEURAL CELLS. M.Cîrstea. "D.Danielopolu" Inst.of Normal and Pathological Physiology, Academy of Medical Sciences, Bucharest, Romania.

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A pharmacologically active factor in egg white (probable a polypeptide of high molecular weight) described recently by us induces a slow-type contraction of the guinea-pig intestine. The behaviour of the contraction when the temperature of the incubation fluid was lowered to 28°C indicates that the egg white factor does not act directly on the intestinal musculature, and hexamethonium did not influence the myenteric neural cells. Atropine indicating that cholinergic mechanisms either at ganglion cell level or at neuromuscular terminals are not involved in this effect. Pretreatment with contraction. Neither histamine nor serotonin represent, therefore, the final chemical transmitter. Crossed tachyphylaxis between substance P and the would represent the final chemical transmitter released by myenteric neural cells upon stimulation by this factor.

A NEW FAMILY OF POLAROGRAPHIC ELECTRODES FOR THE MEASUREMENT OF GLUCOSE, ETHANOL, AMINO ACIDS AND OTHER OXIDASE SUBSTRATES. L.C. Clark, Jr. Children's Hosp. Res. Fndn., Cincinnati, OH, 45229, USA.

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Hydrogen peroxide is oxidized at a platinum anode to give a current (I) \prec to its concentration. About 50 enzymes generate H_2O_2 : $S + O_2$ \rightarrow P + H_2O_2 . Conditions may be set up so that I is \prec to the conc. of S. A working anode is made by trapping a very thin enzyme layer between the Pt and a solute-permeable membrane like Cellophane. This dialysis membrane excludes H_2O_2 -destroying enzymes and creates a stable layer for diffusion and reaction. The necessary O_2 can be supplied by filling the anode with air and having the end permeable to O_2 . Insolubilized enzymes can be incorporated in the Silastic end of the electrode, bonded to the membrane, or coupled to the anode metal. The reference can be placed a distance from the anode when there is a conductive path thru the sample. Interfering polarographic I (e.g. from ascorbate) can be electrically subtracted by a non-enzyme anode. Enzymes are combined to analyze, for example, a disaccharide by conversion to an oxidase substrate.

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I NHIBITION OF SODIUM TRANSPORT IN SUSPENSIONS OF SEPARATED RENAL TUBULE FRAGMENTS BY CONCENTRATED EXTRACTS OF URINE FROM SALT-LOADED MAN. E. M. Clarkson and H. E. de Wardener. Dept. of Med., Fulham Hosp., London, W. 6., U. K.

Concentrated extracts of urine obtained from salt-depleted and salt-loaded man have been prepared after freeze drying and separation on Sephadex columns. Experiments have been performed with extracts which included all fractions eluted from the Sephadex column before the salt peak. The results show that extracts obtained from salt-loaded man have an effect on sodium transport in separated renal tubule fragments. In 11 experiments the mean intracellular sodium concentration of tubule fragments incubated in urinary extracts obtained from the subjects during salt depletion was 48 mEq/l cells and the intracellular potassium was 86. 5 mEq/l cells. The mean intracellular sodium concentration of tubule fragments incubated in urinary extracts obtained from the subjects during salt-loading was 52. 5 mEq/l cells and the potassium was 83 mEq/l cells. These results were significant at the level p < 0.0025 for intracellular sodium and p < 0.025 for intracellular potassium. Other experiments demonstrated that aldosterone has no effect on suspensions of tubule fragments prepared in this way. It is concluded that expansion of the body fluids in man causes a change in the concentration of some substance in the urine other than aldosterone which inhibits sodium transport.

RENAL EXCRETION IN THE HIBERNATING HEDGEHOG. G. Clausen and A. Storesund.

Inst. of Physiology, University of Bergen, Bergen, Norway.

In hibernating hedgehogs the following bladder urine to plasma concentration ratios were obtained: Na 0.18, Cl 0.11, K 6.4, Mg 3.7, urea 28, osmolarity 3.4. Thus the mainly extracellular Na and Cl were conserved relative to the mainly intracellular K and Mg. This is explained by the extensive cell breakdown occuring during the hibernating season when the hedgehog neither feeds nor drinks. During hibernation no increase of [urea], [Na], [Cl] or osmolarity from the renal cortex to the papilla was found. The counter current multiplier system thus appears to be inoperative during hibernation. The hypertonic bladder urine (1.1 0sm/1) sampled from hibernating hedgehogs must therefore have been produced in the previous arousal period.

335 GLOTTIS ORIFICE AND EFFORT DEPENDENT PART OF ISOVOLUME PRESSURE FLOW (IVPF) CURVES.

J. Clément, D. Stanescu, K.P. van de Woestijne. Univ.Clin.St.Rafaël, Leuven, Belgium.

The slope of the effort dependent part of the IVPF curves (near zero flow) is regarded as expressing airway resistance. In 17 healthy subjects we constructed expiratory IVPF curves at 55 % TLC. Only the ascending part of the curves, up to plateau level, was studied. This part can be described satisfactorily by a second degree polynom: $F_{0.50} = aP_{0.50} + bP_{0.50}^{5} + c$. However, an additional highly significant (P<0.01) relationship was detected between $F_{0.50} = aP_{0.50} + bP_{0.50}^{5} + c$. However, an additional highly significant (P<0.01) during the same expiratory maneuver? $F_{0.50} = aP_{0.50} + bP_{0.50}^{5} + cF_{0.50} + cF_$

N-METHYL AND N-DIMETHYLHISTAMINE AS GASTRIC SECRETORY CHEMOSTIMULATORS. C.F.Code, S.M. Maslinski, F.Mossini, and H.Navert. Mayo Clinic and Mayo Fndn., Rochester, Minn., U.S.A.

In a prior study by two of us with Flock and Tyce, N-methylhistamine (NMH) and N-dimethylhistamine (NDMH) were found in gastric mucosa and gastric juice of dogs during constant IV injection of \$^{14}\$C histamine. When administered intravenously, NMH, NDMH, and histamine all produced the same maximal gastric secretion but NMH and NDMH were twice as potent as histamine at the half-maximal level of secretion. When NMH and NDMH were delivered directly to the gastric mucosa via the arterial system, they were 4 to 13 times as potent as histamine when given in equimolar quantities, slowly or quickly, over the dose range of 0.1 to 1 pmole. Aminoguanidine, which enhances the effectiveness of histamine by inhibiting its oxidative destruction, also greatly increased the gastric secretagogue actions of NMH, NDMH, and gastrin. These results (1) establish that NMH and NDMH are more potent chemostimulators of parietal cells than is histamine, and that NMH and NDMH occur in gastric mucosa and juice during stimulation of secretion by histamine, (2) lend support to the prospect that NMH and NDMH are responsible for part or all of the gastric secretagogue action of histamine, and (3) indicate that this pathway may also be used by gastrin.

THE INFLUENCE OF INHIBITORY MECHANISMS IN THE LATERAL GENICULATE NUCLEUS ON THE TRANSFER OF OPTIC TRACT ACTIVITY. A.M.L. Coenen, H.J.M. Gerrits and A.J.H. Vendrik.

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There is evidence that a cell in the lateral geniculate nucleus (LGN) receives input from one single optic tract (OT) fibre. So the responses of units of the two levels are directly comparable. Recordings of the activity of OT and LGN units after visual stimulation were made from non-anaesthetized paralyzed cats. The analysis of these recordings showed three striking differences between OT and LGN responses. 1) The responsiveness of OT units is relatively high and independent of the level of consciousness, while the responsiveness of LGN units is more variable and mostly lower. Only during alertness it approximates the level of OT responsiveness. 2) In the light-adapted state the responses to diffuse stimulation of an OT on-center fibre at light off and an off-center fibre at light on are considerably suppressed in the LGN. 3) The inhibitory pauses are more prominent at LGN level. An explanation of these findings is based on data derived from quasiintracellular recordings of LGN units. These show EPSP's, spikes and hyperpolarizations, so input, output and mode of action of the unit is known. It appears that the input obtained from the quasi-intracellular recordings is indeed equal to the OT activity. Hyperpolarization in LGN units during periods with low excitatory input is responsible for the phenomena given in the points 2 and 3, while the behaviour of responsiveness of LGN units mentioned in point I is caused by an inhibitory mechanism which is probably able to regulate the size of the EPSP's according to the level of consciousness.

METABOLIC RESPONSES OF DOG KIDNEY CORTEX SLICES TO CHANGES IN EXTRA-CELLULAR pH: EVIDENCE FOR A METABOLIC COMPONENT IN RENAL REGULATION OF pH. Julius J. Cohen and David H. Pashley, Univ.of Rochester, Rochester, N.Y.USA

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We have observed that renal metabolism effects a non-excretory form of pH regulation. This is manifest by a change in the metabolic pathways by which certain substrates are utilized: When ECF-pH is high, neutral substrates are metabolized to acidic products which accumulate, tending to lower pH; when ECF-pH is low, acidic substrates are converted to neutral substrates and HCO3 tending to raise pH. Slices of dog renal cortex were incubated in Krebs-Ringer Bicarbonate (95% O2 - 5% CO2) at 30°C. Medium pH was adjusted to 7.0, 7.4 or 7.8 by changing [HCO3]. The 14C-labelled substrates were present at from 1mM to 10mM. 14CO2, glucose, and lactate produced were measured. Fructose and glycerol metabolism were markedly affected by AECF-pH in that at high ECF-pH, lactate was a major product while at low ECF-pH, glucose was the major product. Citrate, on the other hand, was utilized at a low rate at high ECF-pH while at a low ECF-pH more citrate was oxidized to 14CO2 and more glucose was formed. Thus the pathways by which glycerol, fructose and citrate are metabolized tend to buffer the ECF-pH. The quantitative contribution of the renal metabolic pH regulatory mechanism in vivo remains to be determined.

THE DEVELOPMENT OF NEUROMUSUCIAR ACTIVITY IN AMPHIBIAN EMBRYONIC TISSUE CULTURED IN VITRO.

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At early stages of development, and presumably prior to innervation, skeletal muscle cells are sensitive to acetylcholine over their entire length. A widespread sensitivity to acetylcholine also occurs under conditions which allow adult muscle cells to become innervated by regenerating motor nerve fibres. The possibility therefore arises that the action of neurotransmitter on presumptive post-synaptic cells is important in the formation of synapses. In order to examine this possibility neural plate explants from embryos of Kenopus laevis were cultured in vitro. Within 2 days striated muscle cells appear at the periphery of the explants and some of them contract spontaneously. The contractions are reversibly abolished by d-tubocurarine. Intracellular recordings also reveal the occurrence of spontaneous subthreshold depolarizations which are analogous to miniature endplate potentials, thereby indicating that functional neuromuscular junctions have formed. When explants are cultured from the start in concentrations of d-tubocurarine or hemicholinium-3 which prevent any spontaneous neuromuscular activity they develop in the same way as control explants. Upon removal of the drug after 2-8 days spontaneous contractions and subthreshold depolarizations appear. These results indicate that the formation of the neuromuscular junction can occur in the absence of any post-synaptic activity. (Supported by the Medical Research Council of Canada.)

ROLE DE LA PARTIE TERMINALE DU TUBE DIGESTIF DES LAMELLIBRANCHES DANS LES TRANSPORTS D'IONS.

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La partie terminale de l'intestin des Lamellibranches d'eau douce offre la particularité de traverser la cavité cardiaque. Le système circulatoire se trouve séparé par une seule couche de cellules épithéliales du système digestif. Les échanges ioniques à travers cet épithélium ont été étudiés in vitro par perfusion de ce fragment du tube digestif. Un transport actif de calcium dirigé de l'intestin vers le coeur peut être décelé (9,9 .10 $^{-3}\mu Eq/h/cm^2 \pm 2,0$) Simultanément apparaît un flux net de potassium équivalent. L'action de certains inhibiteurs métaboliques (dinitrophénol, ouabaıne, iodoacétamide , cyanures) sur ces transports actifs ont été essayés. Les effets d'un puissant inhibiteur (diamox) de l'anhydrase carbonique, enzyme qui est présente dans ce tissu ont également été étudiés.

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- Adrenergic mechanisms in constriction of cat lungs with histamine. H.J.H. <u>Colebatch</u> and L. <u>Engel</u>, School of Medicine, University of New South Wales, Kensington, Australia.

By exciting contraction of smooth muscle in alveolar ducts, histamine restricts distension of the lung. This action of histamine is antagonized by epinephrine. The effect of histamine on the absolute volume-pressure (V-P) curve of the lungs was studied in cats anesthetized with pentobarbital, paralyzed with gallamine triethiodide and ventilated at a constant rate and tidal volume. Functional residual capacity (FRC) was measured during apnea by a Boyle's Law method after injection of a known volume of gas. In 5 cats with intact adrenal glands, histamine (10 $\mu g/kg$ i.v.) decreased FRC 11% (mean, range 0-21%) and the V-P curve showed a small increase in lung recoil which was reversed by inflation of the lungs to 20 cmH₂0. In 10 adrenalectomized cats histamine (10 $\mu g/kg$ i.v.) decreased FRC 24% (mean, range 14-50%) and increased lung recoil pressure. At a transpulmonary pressure of 6.0 cmH₂0 in 9 cats, histamine reduced lung volume 33% (mean, range 9-53%). The changes were not reversed by inflation of the lungs to 20 cmH₂0, but were reversed by inflation after isoproterenol (3 $\mu g/kg$ i.v.). Histamine decreased FRC to a similar extent whether the lungs had been ventilated with air or with 100% oxygen. The results are consistent with histamine regulating the distensibility of respiratory units in the lung, but provide no evidence of airway closure.

RABBIT OCULAR STABILITY UNDER VARIABLE OPTOKINETIC FEEDBACK CONDITIONS.

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The scarcity of eye movements in the rabbit in normal visual conditions is well known, and was confirmed by quantitative procedures in encéphale isolé preparations. In darkness and after blinding this stability is immediately lost and replaced by irregular smooth drift, the amplitude of which is limited by saccadic reset movements. An 'open loop' condition was created by clamping one eye (the seeing eye) and covering the other eye (the moving eye). In this condition visual feedback is interrupted too, and the moving eye proved to be unstable. By surrounding this preparation with a servo-driven striped drum, position-steered by the moving eye, the seeing eye was provided with information about the movements of the other eye. Using a feedback factor of -1, the moving eye was stabilized by this procedure. A feedback factor equal to +1 strongly enhanced instability. The difference in stability in dark/light and open/closed loop situations can be quantitatively accounted for by known input-output relations of the rabbit's optokinetic system.

DENDRITIC INHIBITION OF SPINAL MOTONEURONS. W.A. Cook, Jr., C.C. Duncan, Jr., and A. Cangiano. Inst. of Physiology, Univ. of Pisa, Pisa, Italy and Div. of Neurosurgury, Duke Univ. Med. Ctr., Durham, N.C.

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The location of inhibitory synapses on spinal motoneurons has been studied in pento-barbital-spinal cats. Electrical stimulation of group II posterior biceps-semitendinosus afferents evoked a long lasting (60-300 msec) inhibitory postsynaptic potential (IPSP) in gastrocnemius-soleus motoneurons. This polysynaptic IPSP could be divided into early and late components on the basis of a differential response to intracellular injections of chloride. As compared with IPSPs of known composition, the late portion of this polyinsensitive to both the intracellular concentration of chloride and induced shifts of the membrane potential. These data suggest that the synapses generating the late portion of the IPSP terminate on the remote dendrites of spinal motoneurons whereas the characteristics of the early portion of the IPSP implicated a more usual somatic termination for the responsible synapses. In further contrast with the early IPSP, the late IPSP did not influence the amplitude or time course of the homonymous monosynaptic excitatory postsynaptic potential (EPSP) which argues for spatial segregation of the synaptic terminals mediating the monosynaptic EPSP and the late polysynaptic IPSP.

CALCIUM DEPENDENT DEPOLARIZING RESPONSES RECORDED FROM CRAB NEUROSECRETORY TERMINALS. I. M. Cooke. Biol. Labs., Harvard University, Cambridge, Mass., U.S.A.

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Intracellular recordings from bulbous neurosecretory terminals of the crab (Cardisoma guanhumi) sinus gland reveal regenerative depolarizing responses which sometimes occur 'spontaneously' and can be elicited by extracellular stimulation of the sinus gland nerve or by current through the recording electrode (Cooke, 1967, Am. Zool. 7, 732). From a usual resting potential of -40 mV the potentials overshoot to + 15 mV. They have durations >10 msec, sometimes have inflections on the rising and falling phases, and have pronounced after hyperpolarizations (10-15 mV, >100 msec). Changing the continuous perfusion from normal (460 mM/1) to 1/2 Na-tris results in abrupt failure in <3 min of response to axon stimulation. Overshooting responses to current persist. Similar results are obtained by perfusion with 10-7 M TTX. Perfusion with '0' Ca saline in many terminals leads to progressive slowing and reduction of amplitude of responses and finally to failure. A small potential, which extracellular recording indicates represents the axonal spike, persists in response to axon stimulation. The effects of these procedures are reversible. While further experiments are needed, these observations suggest that crab neurosecretory axons have Na-mediated spikes while the regenerative depolarizations of the terminals include a major component of Ca current. (Supported by NSF GB 4315X).

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STIMULUS PARAMETERS AND DRUGS IN SELF-STIMULATION. S.J.Cooper, D.Joyce and A.Summerfield. Dept. of Psychology, Birkbeck College, University of London, England.

It has been suggested that self-stimulation performance reflects a rat's attempt to maintain an optimal level of brain stimulation. This problem has been approached using a finer measure of performance than the usual average response rate. Individual interresponse times (IRTs) were recorded for various combinations of stimulus parameters. Square wave stimulation was delivered to the lateral hypothalamus. Four frequency conditions (50, 100, 200, 400 pps) and seventeen stimulus durations (0.03- 1.80 sec) were used. Relative frequency distributions were derived and indicate a predominant frequency mode for durations up to 0.30 sec. irrespective of frequency, that remains the same, despite great changes in average rates. Increasing stimulus strength simply eliminated long 'pauses'. A second mode emerges supplanting the first as duration is increased. Responses here are initiated by stimulus termination, with response suppression during stimulation varying with frequency. For nonaversive stimulation high intensity stimuli lose control and response suppression diminishes as duration is extended. Results implicate separate processes underlying increases in average rates for different parameter combinations. Support is provided by drug experiments. For equivalent low base-line rates amphetamine increased responding at 0.5 sec duration and had no action at low durations whereas amylobarbitone had no effect on self-stimulation with the longer duration stimulus but increased responding at the shorter one. Neural pathways utilising separate neurotransmitters may be differentially involved in the several response modes.

DEVELOPMENT OF AN ASSOCIATION EVOKED RESPONSE IN KITTENS. P. Copack and A.J.

Derbyshire. Dept. of Physiology, University of Illinois at the Medical Center, Chicago, Ill., U.S.A.

The development of an association area evoked response to sound was studied. Long latency, long duration waves (No, P₁, N₁, P₂, and N₂) of an evoked potential to sound were recorded by monopolar electrodes positioned under the skin overlying the parietal association area in Siamese kittens ranging in age from 4 days to 4 months. The sound stimuli consisted of broad and narrow frequency bands of noise with both fast and slow rise times at intensities of 70, 80, 90 and 100 dB. The mean and the variance of 20 responses in each of the 16 sets of stimuli were used to identify the response in each animal. This response could not be recorded until the third week of postnatal life, two weeks after the appearance of the response from the primary auditory area. The amplitude from the peak of N₁ to the peak of P₂ was not age dependent, but was intensity dependent. The

life, two weeks after the appearance of the response from the primary auditory area. The amplitude from the peak of N_1 to the peak of P_2 was not age dependent, but was intensity dependent. The latencies of N_0 , P_1 and N_1 decreased with increasing age, but those of P_2 and N_2 were not affected by age. An increase in intensity, however, caused a decrease in latencies of the N_1 , P_2 and N_2 waves but had little influence on the latencies of the N_0 and P_1 waves. The amplitude and the latency of the response were not influenced by the frequency band or the rise time of the noise. It is concluded that (1) the response to sound recorded from association cortex appears at a later age than the response from primary auditory cortex and; (2) the response consists of two separate elements, a short latency portion perhaps reflecting afferent input and a longer latency portion reflecting central processing.

RHEOGONIOMETRICALLY MEASURED VISCOSITY PROFILES OF PLASMA PROTEIN SYSTEMS AND A NEW CONCEPT OF THE GENESIS OF THROMBOSIS.A.L.Copley.Hemorrhage and Thrombosis Research Labs.,Dept.of Pharmacology,New York Medical College,N.Y. N.Y.10029, U.S.A.

Viscosity of human plasma and serum systems and of solutions of fibrinogen and other plasma proteins were measured with the Weissenberg rheogoniometer in a combined Couette and cone and plate geometry with and without guard ring at varying rates of shear from 10° to less than 10° seccolor Exclusion of surface layer measurements by using the guard ring resulted in Newtonian flow characteristics, while their inclusion without guard ring measured. Towerall viscosity profiles exhibiting non-Newtonian behavior. Marked increase in overall viscosity was found upon addition of 0.4% fibrinogen to 5% plasma or 0.25% albumin, but such addition to 90% plasma or 5% albumin showed no change in non-Newtonian behavior, On the basis of these and other findings a new concept for thrombogenesis is advanced. It postulates formation of polymolecular layers of fibrinogen and other plasma proteins due to their aggregation in an adsorption process first on the endo-endothelial fibrin film, proposed in 1953 by the author (Abst.XIX Physiol.Congr.Montreal) to occur physiologically, followed by a growth process in which additional protein molecules adsorb on the first or previously formed layers of adsorption. Protective colloids as anti-adsorbents are considered to counteract or prevent this thrombosis initiating aggregation of fibrinogen and other plasma proteins. (Aided by the Office of Naval Research, contract NO0014-67-A-0449-0002 and the Veterans Administration Department of Medicine and Surgery Washington, D.C.

MORPHOLOGICAL DEVELOPMENT OF NEURONS IN THE CHICK CEREBRAL HEMISPHERES, CORRELATED WITH THEIR CAPACITY FOR SYNCHRONIZED BIOELECTRIC DISCHARGES. M.A.Corner and A.P.C. Bot. Central Institute for Brain Research, Amsterdam, the Netherlands.

Dendritic development in the superficial regions of the hemispheres between 12 and 20 days of incubation was investigated in Golgi-stained sections. There is enough consistency for qualitative conclusions to be made about the (exclusively stellate) neuronal population. Whereas little correlation existed between cytomorphological changes and the normal ontogeny of bioelectric activity (EEG), a close relationship did emerge when functional capacity was used instead. This variable was measured from maximal "seizures" induced by four convulsive agents: glutamic acid, methionine sulphoximine, metrazol and ouabain. The most prominent pathophysiological feature in all series was the presence of trains of large, surface positive, waves lasting 300-400 msec each. Their maximum amplitude was stage-specific and increased progressively from day 12 to 16, paralleling the increasing dendritic outgrowth. Day 16 to 18, on the other hand, marked a plateau both in dendritic and in pathophysiological maturation. A final large amplitude increase between days 18 and 20 was correlated with the appearance of large numbers of dendritic spines and of greatly increased collateral axon branches, which latter had remained essentially constant at least since 12 days of incubation. Neuronal apacity clearly depended also upon less easily visible factors, since the ontogeny the negative "spike" preceding a wave deviated somewhat.

STRUCTURAL REQUIREMENTS FOR THE ACTION OF THE OXYTOCIN MOLECULE ON SODIUM EXCRETION AND TRANSPORT ATPase. J.H.Cort, E.Sedlakova and T.Dousa, Laboratory for Peptide Biology, Academy of Sciences, Prague, Czechoslovakia.

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Oxytocin analogues have been prepared in which the following structural changes have been made: 1) alterations in ring size and the number of sulphur atoms contained therein and 2) substitution of polar amino acids by aliphatic ones in the ring structure. The activity of these analogues has been tested on a) natriuresis in the chloralosed cat preparation, b)"transport"-ATPase prepared from rabbit kidney cortex and c) Na ejection from cold-loaded rabbit kidney cortex slices. An increase or a decrease in ring size decreased natriuretic activity both in terms of duration and amplitude. Aliphatisation of the ring in sequence positions 3 & 4 not only resulted in a marked increase of both amplitude and duration of natriuresis, but also resulted in compounds which inhibited Na-K-activated-ATPase activity and Na ejection from loaded slices, all in association with a sharp decrease in pressor activity. Tritiated oxytocin binds to the "transport"-ATPase membrane fraction at a level of 5 x 10 Mole/mg total N - addition of natriuretic analogues to the same reaction mixture prevented this binding. The theoretical and practical consequences of these observations will be discussed.

MECHANICAL AND PHYSIOLOGICAL ASPECTS OF ROWING. G. Cortili, P.E. di Prampero, F. Celentano and P. Cerretelli. Inst. of Human Physiology, University of Milan, Italy.

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The forces acting upon the oarlock and the mechanical power developed during rowing have been measured in different conditions together with heart rate, O₂ uptake and lactic acid production of the subjects. It has been calculated that about 0.14 of the total energy expenditure is lost by the best athletes and even a higher fraction by the less skilled subjects. This may be attributed mainly to the fact that about 0.21 of the force exerted by the rower is wasted as it is acting perpendicularly to the direction of the progression. The force wasted may possibly be reduced to 0.11 by correcting the geometry of the system. The mechanical power necessary to maintain the progression of the shell increases with the 3.6 power of the mean speed. This increase can be obtained by increasing either the frequency of the strokes, or the work per stroke. The efficiency of rowing is of the order of 0.18 at low rowing frequencies (<25 strokes/min); at higher rates it increases up to a value of about 0.23, which appears to be constant in the investigated range of frequencies (<37 strokes/min).

MUSCLE TRANSPLANTS IN NORMAL AND DYSTROPHIC HOSTS. $\underline{\text{E. COSMOS}}$ and $\underline{\text{J. BUTLER}}$. Institute for Muscle Disease, Inc., New York City, N.Y., U.S.A.

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Our studies with muscles from chickens with hereditary muscular dystrophy have indicated that the disease is expressed as an inability to differentiate white muscle. Since existing evidence implicates neurotrophic influences on the differentiation of fiber types, it seemed reasonable to investigate neuronal substances in the evolvement of the dystrophic process. To test this role of extra-myogenic influences, the undifferentiated pectoralis from dystrophic chickens was removed at day 1 ex ovo, minced, and exchanged for the same muscle of a normal bird. The left pectoralis of each bird was left intact as a control. Preliminary results indicate the following: 1) In a comparison of the birds as hosts for muscle transplants the dystrophic chicken excels in its ability to retain and to develop muscle from a donor bird. 2) Normal tissue transplanted to a dystrophic host retains normal characteristics during maturation; likewise, dystrophic muscle in a normal host is unaffected by the normal environment. 3) By 25 weeks of transplantation the normal mince in the dystrophic host shows a 70- to 90-fold increase in weight; the dystrophic mince in the normal host is completely rejected. These experiments present strong evidence that the dystrophic process is of myogenic origin and that it appears to be unaltered by extra-myogenic influences. Supported by a grant from Muscular Dystrophy Associations of America, Inc., and by USPHS award NS-06942-04.

CHANGES IN THE PROTEOLITIC ACTIVITY OF THE GASTRIC JUICES DURING THE ADMI-NISTRATION OF CINCOPHEN. J. Fernández Costa. CENIC Sch. Med. Univ. Havana. Inst. Gastroenterologia. MINSAP. Apartado 6990. Havana. Cuba. 352

Gastric Secretion was stimulated using meat in dogs carrying pouches and fistulae by modification of the "fictive meal" technique. The proteolitic activity of gastric juice was determined by the haemoglobin technique at ten different pH with whose outcome activity curves between pH 1 and pH 5 were traced. During the control period, all animals curves exhibited two peaks but after the administration of Gincophen(oral, 0.25 g/kg) was started three peaks similar to those reported by Taylor-W.H. 1959 and was started three peaks similar to those reported by Taylor-W.H. 1959 and 1962 in humans. When we stopped administering Cincophen the proteolitic activity returned to normal. Treatment with Cincophen was repeated on the same dog on two further occasions and the return to normal proteolitic activity ocurred also. It was also studied the latency and secretion volume; pH, free and total acidity; presence of blood in juice and faeces and raised levels of histamine in the blood.

ELECTROPHYSIOLOGICAL CORRELATES OF STRUCTURAL MODIFICATIONS OF BRAIN TISSUE BY ENZYMES AND BY ANTIGEN-ANTIBODY REACTIONS TO CNS PARTICULATE FRACTIONS. Anatol Costin, Dennis R. 353 Hafemann, Theodore J. Tarby, Carl Cotman and Harvey R. Herschman. Brain Research Institute, University of California, Los Angeles, USA.

Cats with chronically implanted electrodes and cannulae were used. The enzymes phospholipase A (0.14 U), phospholipase C (0.16 U), and pronase (0.45 U), when introduced directly into the lateral geniculate body of the cat brain, bring about decreases in EEG amplitude, flash evoked potential amplitude and tissue impedance. The enzyme hyaluronidase (225 U) increases the spontaneous EEG amplitude and causes seizure activity without changing evoked potential amplitude or tissue impedance.

The specific antisera to rat nerve ending (anti-nerve ending particle antibody) (anti-NEP) prepared in rabbits, when introduced into the lateral geniculate body of the cat brain, produces small increases in tissue impedance. The "complement" (guinea pig serum), on the other hand, brings about decreases in photic evoked potentials and tissue impedance. The effect of the "complement" is prevented by prior application of anti-NEP. Control rabbit antisera to a non-neuronal antigen (myosin) or anti-NEP previously absorbed with isolated rat nerve endings do not appear to inhibit the effect of the "complement" on both impedance and evoked potentials.

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CORONARY ADRENERGIC HAEMODYNAMIC RESPONSES. R.L.Coulson. Dept. of Physiology, University 354 College London, London U.K.

The steady state effects of intravenous adrenaline infusions on blood pressure, flow, resistance and heart rate in both the pre and post network sectors of the coronary circulation were investigated with and without pre-treatment with 0.5 mg/Kg propranolol before and after occlusion of a branch of the left anterior descending coronary artery in Nembutal anaesthetized closed-chest dogs. The following results were obtained:- 1. Adrenaline increased pre and post network blood flow and pressure (both mean and pulse). It decreased pre-network resistance but post network resistance was not altered, nor was heart rate. Propranalol reduced pre and post network blood flow, increased pre and post network resistance and depressed heart rate. 3. Occlusion reduced pre network but did not change post network pressure. It depressed post but not pre network flow. There was no change in resistance or heart rate. 4. Combined propranalol and adrenaline increased post net pressure more than the sum of the effect of each agent individually. Heart rate depression was also synergic. The primary vascular control of coronary blood flow is thought to reside in pre network resistance vessels. Post network vessels do not normally participate in maintenance of adrenergic vasomotor state but became important after occlusion in determining blood flow redistribution through the anastomotic network.

AIRWAY CLOSURE AND ALVEOLAR-ARTERIAL O₂ DIFFERENCES IN MAN. J. Couture, F. Ruff, E. Housley, D. Craig, H. Don, M. Becklake and J. Milic-Emili. Dept. of Physiology and of Anaesthesia, McGill University, Montreal, Canada.

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Recent studies have shown that increasing age and/or body weight result in airway closure in the dependent lung zones, particularly in the supine position. The present study was designed to assess quantitatively the effect of airway closure on pulmonary gas exchange. In 40 normal and 22 obese subjects, whose age ranged from 18 to 77 years, we have measured (a) the (A-a)DO2 and (b) the difference between the functional residual capacity (FRC) and the "closing volume" (CV). Measurements were made in both seated and supine positions. "Closing volume",i.e.,the lung volume at which the dependent airways begin to close was measured by the 133 xe ionship between (A-a)DO2, in mmHg and FRC-CV, expressed as a percentage expression:

(A-a)DO2 = 15.8 e -0.05(FRC-CV)

The above relationship applied in both normal and obese subjects, independent of their age and position. It is concluded that the (A-a)DO2 increases exponentially with decreasing FRC-CV, the latter being an expression of the degree of airway closure. (Supported by M.R.C. of Canada.)

HORMONAL INFLUENCES ON SODIUM TRANSPORT BY AMPHIBIAN EPITHELIA INCUBATED IN HYPOTONIC MEDIA. J. Crabbé and A. Decoene. End. Unit, Dept. Physiology, U.C.L., Louvain, Belgium.

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Transport of Na by frog skin is enhanced by exposure of inner surface in hypotonic Ringer's (MacRobbie and Ussing). This has been found to apply to toad (<u>Bufo marinus</u>) bladder, colon and skin. Stimulation of sodium transport by such epithelia can be brought about by aldosterone (A), vasopressin (ADH) and insulin (I) in vitro; these hormonal effects were not modified in a uniform way by incubation in hypotonic fluid. When matched pieces of toad skin were treated with A or I, or left untreated (U), sodium transport (µA/cm²) averaged 15.7, 12.0 and 8.0, respectively, in Ringer's (x=0.225); during the 2nd hour of exposure to dilute Ringer's (x=0.150), corresponding values were 18.1, 18.1 and 9.6 (N=6). After incubation of toad bladder overnight in the presence of A, Na transport averaged 12.4 vs. 4.6 for matched U, in Ringer's; upon dilution of the latter, values were 18.1 and 8.5, respectively (N=8). With fresh toad bladder, Na transport in Ringer's averaged 21.4 before, 39.8 during the hour following ADH; while corresponding values were 29.2 and 55.9 for matched preparations exposed to dilute Ringer's (N=5). Thus, neither A nor ADH increased the (relative) response of these epithelia to hypotonicity; only I did. This is compatible with the hypothesis that I, unlike A and ADH, acts beyond the apical cell border which is the structure supposedly influenced by hypotonicity. Changes seen with glucose-containing media suggest, however, that action of A is not limited to permeability effects at the

MEMBRANE PROPERTIES OF THE SMOOTH MUSCLE CELLS OF THE GUINEA PIG URINARY BLADDER. K.E. Creed. Dept. Physiol., Kyushu Univ., Fukuoka, 812. JAPAN.

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Longitudinal muscle bundles of the urinary bladder were studied with micro-electrodes. The mean resting potential was 37.3 mV in hypertonic Krebs solution and spontaneous action potentials with overshoots of up to 20 mV occurred either continuously or in bursts. Extracellular stimulation elicited spikes which were conducted at a mean velocity of 41.2 mm/sec. Electrotonic potentials decayed exponentially with distance with a length constant (λ) of 1.70 mm. The time constant of the membrane (γ_m) calculated from the electrotonic potential or from the conduction velocity and foot of the spike was 120 - 130 msec. The amplitude and rate of rise of the spike depended on (Ca in the perfusing fluid. Na-deficient solution (γ_m) na tris) produced depolarization and increased membrane resistance. The rate of rise but not the amplitude of the spike was reduced. Increase in (Ca restored the resting and action potentials to normal, suggesting that the spike is due to influx of Ca across the membrane. The smooth muscle of the urinary bladder can therefore be classified as a single unit smooth muscle and resembles other visceral smooth muscles in biophysical properties but differs in the effect of Na-deficient solution.

358 OCULOMOTOR AND VESTIBULAR INFLUENCES ON SUPERIOR COLLICULUS NEURONS. M. Crommelinck and A.Roucoux. Lab. de Neurophysiologie, Université de Louvain, Louvain, Belgium.

The influence of oculomotor activity, either spontaneous or nystamic on activity of collicular neurons has been studied in "encéphale isolé" curarized cat. Nystamus was produced by labyrinthine polarization. Mass potentials at the level of abducens nucleus were recorded as cues of oculomotor orders. Visual input was investigated by means of light and dark stimuli hand-moved on an evenly lit background. The following effects have been observed: (1) phasically correlated discharge (and rarely inhibition) to spontaneous oculomotor activity in about 15 % of recorded neurons; (2) phasically correlated activation (and less often inhibition) to nystamic oculomotor discharges directly observed in about 10 % of collicular units, these effects are labile and apparently submitted to uncontrolled factors; (3) tonic activation, inhibition or changes of firing pattern occurring only during bursts of nystamic waves in less than 10 % of units. It is to be noted that all these modifications have been observed in non visual units as well as in visual ones, though no actual displacement of image on retina occurred in the latter case. Several units are phasically correlated to spontaneous as well as nystamic discharges. All the affected units are diffusely spread in the various collicular layers with no clear distribution pattern evidenced.

TORTOISE MUSCLE SPINDLES. Alan Crowe of Zoology, Univ. of Durham, England.

Spindles in the extensor digitorum brevis I muscle of the tortoise Testudo graeca contain only one type of intrafusal muscle fibre according to observations upon size, nuclear-distribution, ultrastructure and histochemistry. No monofibrillar spindles have been found. The mean number of intrafusal fibres found in a single spindle is 9.7 (range 2-19). The spindle does not contain a bulbous fluid-filled capsule at its equatorial region. Instead, the capsule consists of layers of connective tissue cells between which are collagen fibres. Only one type of sensory ending is found. Each spindle has one sensory nerve fibre. The motor innervation is supplied by collaterals of nerves to the extrafusal fibres. Both plate and grape endings are found, but not always on the same spindle. Preliminary physiological investigations indicate that there is little adaptation in response to mechanical stretch.

360 ITRANSPORT OF MICROSPHERES IN THE GENITAL TRACT OF THE FEMALE RABBIT. H.B. Croxatto, C. Vogel, J. Vasquez. Inst. Ciencias Biol, Univ. Católica, Santiago, Chile.

Egg transport in the genital tract of the rabbit occurs normally under the hormonal conditions that prevail after ovulation. In order to study the transport under other phy-, siologic hormonal levels, a substitute of the egg was used. Microspheres of 76 - 198 μ diameter were injected into the peritoneal cavity of rabbits that were either estrous, mated, castrated or treated with microdoses of megestrol acetate (AM). Animals were killed 24, 48, and 72 hrs. after the injection. The oviducts, divided in three equal portions, the uterus and vagina were flushed to determine the number of spheres in each segment. It was found that the spheres were picked up in large quantities by the fimbria from the peritoneal cavity. Transport occurred at the same rate as that of the eggs in mated animals. In oestrous rabbits the transport was faster than in mated rabbits, not only in the oviducts but also in the uterus. Treatment of oestrous rabbits with MA slowed down the speed of transport. Usually 80 % of the spheres were found in a single segment in hormone stimulated animals, whereas in castrated rabbits they spread through various segments. It is concluded that physiologic levels of estrogen organize the activity of the oviduct so that spheres or eggs are transported toghether. The addition of physiologic levels of progestins slows down the transport beyond the isthmo-ampullar junction.

A SMOOTH MUSCLE MEMBRANE CHARACTER CHANGE DUE TO NUTRITIONAL DYSTROPHY. A. O. Cruz and Y. C. Chang Fisiologia, Universidade Federal do Parana, Curitiba, Brazil.

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Resting membrane potentials, E_m , measured from the longitudinal smooth muscle of rats vasa deferentia raised on vitamin E deficient diet by conventional microelectrodes in normal Tyrode solution was lower(63.1 \pm 1.5 mV) than that measured from the rats raised on normal ration(72.2 \pm 2.2 mV) of the same age(3.7 \pm 0.1 months). The membrane of the deficient group depolarized in increasing (K)₀ in a straight line of 50 mV/10 log(K)₀ slope while that of the normal group depolarized in a curve characteristic of all smooth muscles. Change of (Na)₀ or (Cl)₀ did not appear to modify E_m from either group while increasing (Ca)₀ slightly hyperpolarized that of the normal group and depolarized that of the deficient. Adrenalin did not affect the E_m from either group up to a concentration of 5 x 10 -5w/v while noradrenalin could depolarize that from the deficient(from 10-6 w/v on) but not the normal. T_h ese results indicate a synaptic membrane reaction to nutritional dystrophy by increasing its sensitivity to the transmitter substance and an extrasynaptic membrane reaction by decreasing its resting g_{Na} or increasing the g_K , accentuated by the secondary effect of i_{Ca} . (Supported by CAPES Grant No. 16.447/67 and Cons. Nac. Pesq. Grant No. 8475/67).

AIRWAY RESISTANCE AT SEA LEVEL AND AT HIGH ALTITUDES. Julio C. Cruz. Inst.Invest. Altura, Univ. Peruana Cayetano Heredia, Lima, Porú.

The mechanics of breathing has not been studied previously in high altitude (H.A.) natives. Using the airway interruption technique, we have determined the airway resistance (Raw) in two groups of subjects: 1. Natives at 4300 meters of altitude and after descent to sea level (S.L.), and 2. S.L. residents before and after arrival to the altitude mentioned. Fourteen subjects were studied, 6 from S.L. and 8 from H.A.

The results are summarized in the following table: N° Raw at V=1 lit/sec. Birtholace Place of $\Delta P = K_1 \dot{V} + K_2 \dot{V}^2$ of subjects the study subjects (cm.H20/1/sec.) Kı 2.46 ± .32 S.L. 6 3.04 ± .19 .58 ± .15 H.A. 6 2.84 ± .28 $2.06 \pm .30$.79 + .162.72 ± .15 2.47 ± .19 H.A. 8 2.13 ± .19 .60 ± .15 1.86 ± .18 H.A. 4 .61 ± .11 S.L. 4 $3.00 \pm .21$ 2.18 ± .21 $.83 \pm .26$

The data show that all S.L.subjects, but one, decreased the Raw when they were exposed to H.A. Four H.A. subjects did the opposite on descent to sea level. However the changes observed in both groups suggest the presence of a certain degree of bronchoconstriction while at H.A. There was not significant difference between the two groups at any of the two levels studied. (Supported in pert by U.S. Army Research Grant DA-HC19-68-G-0030).

SENSITIVITY TO PROTEASES AND ANAPHYLACTIC PROTEASE PRODUCTION IN ADRENALECTOMIZED RATS. B. Csaba, L. Muszbek and K. Kovács. Dept. of Pathophysiology, Univ. Med. Sch., Debrecen, Hungary.

The susceptibility of rats to shock produced by proteases /pronase, trypsin/ was increased by adrenalectomy. A significant elevation was shown in acid protease activity in the serum during passive and active anaphylaxis. A moderate rise was observed in neutral protease activity during active anaphylactic shock only. Adrenalectomy alone did not influence either the acid or the neutral serum protease levels in rats. However, a further increase in lysosomal acid protease activity and a significant rise of neutral protease level could be detected in adrenal-ectomized animals undergoing to anaphylaxis. These mechanisms may play an important role in the pathogenesis of increased sensitivity caused by adrenalectomy.

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EXPERIMENTAL DATA ON THE SO CALLED PERIVASCULAR SPACE IN THE BRAIN.

E. Csanda, Z.Ö.Zoltán, I. Dobranovics and A. Szücs. Neuropsychiatry of the Medical University of Szeged, Szeged, Hungary.

Experiments on cats and dogs were performed with a./supravital perfusion technic; b./tracer method introducing different substances into the brain and in the subarachnoidal spaces /SAS/; c./blocking the lymphatics of the neck. The brain and adjacent tissues were examined macroscopically with Cytoplast, microscopically with light- and electronmicroscopical technics. The investigations prooved: 1./The classical perivascular space - declared by many authors as artefacts - does not exist in normal conditions. But in different pathological states gaps are produced between the astrocytic foot and the adventitia of the vessel wall. 2./Intradventitially, between the outer layers, there are semicircular-like gaps, visible only if they are filled with lymph-due substances - or after blocking the lymphatics of the neck. These correspond morphologically to the classical Virchow-Robin spaces, physiologically to the para-, or prelymphatics known elsewhere in the body. 3./The SAS is connected only to the intraadventitial gaps of greather vessels, both arteries and veins.

RESPIRATORY STUDIES IN WOMEN AT HIGH ALTITUDE (3600-5200 M. or 12,200-17,100 Ft.).

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Paz, Bolivia; Div. of Res., Lankenau Hosp. and Jefferson Univ. Sch. of Med., Phila., Penna.

At both altitudes and at rest resident native women showed higher PACO2 and paCO2 and lower PAO2 and paO2 as well as lower arterial pH than native males. These differences were statistically significant. Resting VE/BSA (minute volume), VT (tidal volume) and (f) (respiratory frequency) were similar. The differences in the native females stem from larger VDS (dead space), VDS/VT and reduced VA (alveolar ventilation). Newcomer females, resting at both altitudes, differed from newcomer males in regard to larger VE/BSA, VA and (f), while VT was smaller. VDS and VDS/VT and VO2/BSA (oxygen consumption) were of similar size. These differences were also reflected in lower PACO2 and paCO2, higher PAO2 and paO2 and increased ventilatory equivalents for oxygen (VE/VO2 and VA/VO2). Native females contrasted with resting female newcomers at 3600 M. showed higher VE/BSA, VT, PACO2 and paCO2, lower paO2 and arterial pH, reduced VA and larger VDS and VDS/VT. Both at 3600 and 5200 M. newcomer females during steady-state 60 watt (376 Kg./M./min.) exercise showed lower PACO2 and paCO2, higher pH and smaller VDS and VA/VO2 and VE/VO2 than exercising native females. The latter differ from exercising native males at same work load in that VE/BSA and VA are reduced, PACO2 and paCO2 are higher, PA-aO2 gradients are wider, pH is lower and VDS and VDS/VT are larger. Contrasted with newcomer females during steady-state exercise at both altitudes newcomer males showed consistently smaller VDS, larger VA and lower paCO2.

COMPARATIVE THERMOREGULATORY RESPONSES OF MEN AND WOMEN DURING PERIODS OF INDUCED THER-MAL TRANSLETTS. D. J. Cunningham and J. A. J. Stolwijk, Inst. of Health Sciences, Hunter College, CUNY, N.Y. 10021, and John B. Pierce Fndn. Lab., New Haven, Conn. 06519, U.S.A.

Resting male and female subjects were exposed in a climatic chamber to an ambient temperature of 30°C for 10 mimutes, following which time the room temperature was elevated over a period of 60 mimutes to ca. 48°C and then lowered to ca. 15°C over the next hour. Tympanic temperature, ten skin temperatures and ten local thermal conductance rates were recorded once each minute. Metabolic rate was measured periodically while categorical evaluation of thermal sensation and relative discomfort were made by the subject at regular intervals. A continuous record of weight loss was also obtained.

The subjects achieved a near steady state in response to the 60 minute exposure to a 48°C ambient and essentially no steady state was reached during the cooling period. Skin temperature excursions were greater in the women than in the men; sweating occurred later and at a lower rate in women. Thus during heating, sweating was more pronounced, and vasodilatation was less pronounced in men than in women. On the other hand, shivering and vasoconstriction as a response to the 15°C environment were more pronounced in women. Discomfort magnitude estimates were correlated with physiological responses: men tended to report discomfort in the heat earlier than the women, whereas in the cold, women tended to report discomfort earlier and of higher magnitude than men.

STUDIES ON THE PATHOGENESIS OF CALCIUM CHLORIDE-INDUCED CARDIAC ARRHYTH-MIAS. B.Cuparencu, I.Ticsa, L.Safta, V.Csutak, Tereza Barzu and R.Mocan. Dept. of Pharmacology, Faculty of Medicine, Cluj, ROMANIA.

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I.v. infusion of 5% CaCl₂ solution in chloralose-anesthetized dogs induced ventricular fibrillation at a peripheral venous plasma calcium level of 22.5 ± 6.9 mEq/l and the cardiac plasma calcium level of 22.5 ± 6.9 mEq/l and the cardiac plasma calcium level of 25.5 ± 5.9 mEq/l. The transections of spinal cord at D₁ - D₂ level, but not at C₁ - C₂ level increased significantly cardiac fibriliatory calcemia, but failed to affect peripheral calcemia. The same results were obtained after splanchnicectomy. Pretreatment of animals with reserpine, dl-propranolol, d-INPEA, LB 46 afforded a significant protection. Previous administration of atropine, physostigmine, l (-) IPMEA, d(+) IPMEA and sotalol failed to affect the fibrillatory calcium level. From these results it was concluded that the pathogenesis of calcium chloride-induplayed by the adrenergic nervous system. Calcium chloride could release catecholamines from adrenal medulla and other adrenergic structures affecting the fundamental properties of the myocardium, enhancing the appearance of ventricular fibrillation.

COMPARISON BETWEEN THYROID AND SUBMAXILLARY IODINE PUMPS IN MALE AND FEMALE A2G MICE. H.Curbelo, A.Houssay and E.Bozzolo. Cátedra de Fisiologia, Facultades de Medicina y Odontología, Universidad de Buenos Aires, Argentina.

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I-131 and Tc-99 kinetic studies were performed in normal male and female A2G mice. I-131 studies were also performed in male and female A2G mice after blocking the thyroid with the administration of methylmercaptoimidazol (3 mg three times a day during 4 days). The organ/plasma ratios and the isotope uptake (%) in thyroid and submaxillaries were measured 1,4,8,24 and 48 hours after the tracer dosis. There was a marked sexual difference in the thyroid/plasma and submaxillary/plasma ratios being higher in males than in females. The I-131 thyroid uptake (%) has a peak at 24 hours but the I-131 submaxillary uptake (%) has a peak at 4 hours. The Tc-99 uptake (%) was much greater in submaxillaries than in thyroids due to the different size of the glands. The plasma Tc-99 activity decreased much faster than the Tc-99 thyroid and submaxillary activities, which indicates relative retention of Tc-99 by both glands. Similar results were obtained in the I-131 studies in the methyl mercaptoimidazol blocked mice with greater relative retention of this isotope.

FRUCTOSE POTENTIATION OF INSULIN SECRETION BY THE PERFUSED RAT PANCREAS. Donald L. Curry, Katherine P. Curry, and Maritza Gomez. Dept. of Physiol. Sciences, Univ. of Calif., Davis, Calif. 95616, USA.

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It was found that fructose (300 mg/100 ml) does not stimulate insulin secretion in the absence of glucose. When glucose is present in the perfusing medium at a concentration of 50 mg/100 ml, fructose (300 mg/100 ml) is still ineffectual in stimulating insulin release. However, when glucose is present at a concentration which is sufficient to stimulate insulin secretion, but not insulin synthesis (150 mg/100 ml), the introduction of fructose results in a potentiation of insulin release. This potentiation is characterized by the typical diphasic pattern of insulin secretion...an early burst of insulin release followed by a second slowly rising phase of release (which has been linked to insulinogenesis). It was also found that in the presence of cycloheximide (1 mg/ml) the potentiatory effect of fructose which results in the rising phase of secretion is greatly reduced, however the early burst of secretion is unaffected. Assuming that fructose potentiation occurs via an action on the glycolytic pathway, then these data strongly suggest that the glycolytic pathway is an important intermediary in the initiation of insulin synthesis, as well as insulin secretion.

CHANGES IN CASTRIC MUCOSAL BLOOD FLOW IN CONSCIOUS DCGS AFTER FEEDING. B.F. Curwain & Pamela Holton. Dept. of Physiology, St.Mary's Hosp.Med.Sch., London, England. 370

Although it is generally assumed that gastric mucosal blood flow increases in response to feeding, few quantitative data are available. We have investigated the magnitude and time course of changes in gastric mucosal blood flow in conscious dogs after a standard meal and have related these changes to the rate of acid secretion. Gastric mucosal blood flow was measured by the clearance of radioactive aniline (Curwain & Holton, 1971) in conscious dogs equipped with separated and vagally innervated gastric pouches. Acid secretion was also measured. Control experiments showed that the acid secretion was unaffected by the aniline used. Aniline clearance increased parallel with acid secretion from separated pouches. In dogs with vagally pouches aniline clearance increased before acid secretion rose. It is concluded that gastric mucosal blood flow increases within a few minutes of starting to eat, and remains at a high level throughout the cephalic and gastric phases of acid secretion. Initial increase in mucosal blood flow precedes secretory response.

This work was supported by the Medical Research Council. Ref. Curwain, B.P. & Holton, Pamela. 1971. Proc. of the Br. Phermac. Soc., January 1971.

BLEEDING TIME AS A VEGETATIVE CORRELATE OF INCREASED EMOTIONAL TENSION. J. Cytawa and J. Domańska. Dept. of Animal Physiology, Curie-Skłodowska 371

Univ., Lublin, Poland.

Increased emotional reactivity caused by electrolytic lesion of the septal forebrain area in rats is accompanied by a marked shortening of the bleeding time which lasts throughout the period of the septal synthemical synthemical septal synthemical septal synthemical septal synthemical synthemical septal synthemical septal synthemical synthemical septal synthemical septal synthemical synthemi the bleeding time which lasts throughout the period of the septal syndrome and shows a highly significant negative correlation with the emotional reactivity. A distinct shortening of the bleeding time is also a concomitant of other states of increased emotional tension, such as examinational emotion in students and immobilization stress in rats. As the emotional shortening of the bleeding time is accompanied neither by appropriate changes in the blood clotting time nor in the blood platelet count, it seems to be mainly of vascular origin. Since the serum from rats subjected to brief stress causes a marked shortening of the bleeding count, it seems to be mainly of vascular origin. Since the serum from rats subjected to brief stress causes a marked shortening of the bleeding time when injected to the test animals, while the serum from rats exposed to long stress or from rats showing the syndrome of septal hyperemotionality causes a pronounced lengthening of the bleeding time, it follows that during emotional vasoconstriction, evoked by both nervous and humoral mechanisms, a strong vasodilatatory substance gradually appears in the blood. Their amount increases with the prolongation of the emotional tension. sion.

FUNCTION OF GIANT AXONS IN THE ESCAPE RESPONSE OF THE COCKROACH. D.Dagan and 372 I. Parnas. Dept. of Zoology, Hebrew University of Jerusalem, Israel.

Giant axons of the cockroach, previously thought to be interneurones activating leg motoneurones during escape, were found to be continuous throughout the nerve cord and not associated with leg motoneurone activation Preparations with degenerated giant axons show activity in the crural nerves triggered by abdominal stimulation. It was found that cercal nerve stimulation activates simultaneously giant and small axon pathways. Information ascending the cord via giant axons apparently inhibites activity which may interfere with escape behaviour, furthermore this information activates antennal movements after reaching the cerebral ganglia. Simultaneously the smaller axon pathway conducts information to leg motoneurones in thoracic ganglia. Microelectrode recordings from the metathoracic ganglion indicate that the giant axons exert their inhibitory effect via interneurones that receive input also from sensory fibers in the crural nerve.

PACEMAKER ACTIVITY IN ISOLATED BUNDLES OF SMOOTH MUSCLE OF THE FROG STOMACH.

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Mechanical and electrical activity of the circular muscle of the frog stomach has been studied. With external electrodes spontaneous electrical activity could be detected only in a small portion of the bundle, extending 6 mm to each side of the controlling pacemaker region. In long bundles at least two pacemaker regions of regular activity were identified, which may result in an irregular total activity of those bundles. The areas which were controlled by adjacent pacemakers were overlapping.

Artificial pacemaker regions could be produced by successive short applications of potassium-rich Ringer solution to any small part of the bundle. Electrical activity spreads from those regions over the same distance as from natural pacemakers regardless of the location of the artificial pacemaker. These results suggest a limited propagation of activity in bundles of smooth muscle which is not due to morphological specialisations in certain regions.

SYMPATHETIC VASOCONSTRICTION OF BRAIN BLOOD FLOW. Louis G. D'Alecy and Eric O. Feigl, Physiology and Biophysics Dept., Univ. of Washington, Seattle, Wa. 98105, U.S.A.

The effect of sympathetic stimulation on cerebral blood flow was investigated in chloralose anesthetized dogs. A new preparation has been developed for the moment to moment measurement of cerebral venous outflow with an electromagnetic flow transducer on the retroglenoid vein. Communication between the dorsal and ventral cerebral sinuses was prevented by occluding the sigmoid sinuses. Blood flow from the base of the cranium and the orbit drained via the vertebral and internal jugular veins. The brain's arterial supply was left undisturbed. The sympathetic innervation of the cerebral vessels was stimulated at the stellate ganglion (3-5 volts, 3 msec, and 1,3,6,10, and 15 Hz for 90 sec.). Stimulation at 15 Hz decreased cerebral blood flow 80%. The vasoconstriction was graded, increasing with the frequency of stimulation from 1 to 15 Hz. During stimulation arterial oxygen tension decreased from 93.2 mmHg to 84.9 mmHg, carbon dioxide tension increased from 32.8 mmHg to 34.8 mmHg, and pH decreased from 7.392 to 7.378 units (avg. of 27 determinations). These changes in blood gas parameters all oppose the observed vasoconstriction. Cerebral spinal fluid pressure increased 6.6 mmHg during sympathetic stimulation. Manually increased spinal fluid pressure (by saline infusion in cisterna magna) to 50 mmHg did not change cerebral blood flow. Opening the cranium to the atmosphere had no effect on the vasoconstriction. In conclusion, sympathetic cerebral vasoconstriction has been demonstrated which is independent of changes in arterial PO2, PCO2, pH and cerebral spinal fluid pressure.

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MODIFICATION OF ACTIN BY NATURAL TROPOMYOSIN. P. Dancker, Max-Planck-Inst. f.med.Forschung, Abt.Physiologie, Heidelberg, Western Germany

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Actomyosin, the contractile ATPase of which can be inhibited by Ca removal consists of myosin and a specific complex between actin and the tropomyosin-troponin-system (natural tropomyosin). This hypothesis is based on the following observations: (1) Natural tropomyosin will combine with actin but not with myosin. (2) From an extract of usual acetone powder of actin a preparation is obtained, which, after the precipitation of polymerizable actin forms with myosin a highly active Ca-dependent contractile ATPase. This preparation consists of natural tropomyosin and a small proportion of actin. It will be bound by myosin, presumbably by its actin part, because pure actin acts as a competitive inhibitor. Tryptic digestion of the preparation reduces the contractile ATPase and abolishes Ca-sensitivity. This means: Natural tropomyosin not only sensitizes the contractile ATPase of actomyosin against Ca but in addition modifies actin in such a way that the actomyosin ATPase which is formed after combination with myosin is more active than that of synthetic actomyosin of the same actin content of purified actin.

RECHERCHES SUR LE RÔLE DES RECEPTEURS EN IMMUNOGENESE. Ermila Daneliuc.
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l'Académie des Sciences Médicales, Bucarest, Romania.

Dans les travaux précédents (Gr.Benetato et col.Rev.Roum.Physiol.1969, 6,3,185 et Rev.Roum.Physiol.1970,7,3,181) on a trouvé dans l'hypothalamus antérieur des neurones qui répondent à l'excitation antigénique, qui sont en même temps thermosensibles. Mais on signale également des neurones qui répondent à l'excitation antigénique, sans être thermosensibles; ceux-ci pourraient jouer un rôle important dans l'immunogenèse. L'exploration des neurones de l'hypothalamus antérieur de lapins de Nouvelle Zéelande non-immunisés, après l'excitation des récepteurs périphériques de l'ilèon avec la circulation isolée, par l'endotoxine typhi murium, met en évi dence l'existence de certains neurones qui répondent avec une latence deux fois plus grande qu'à l'excitation antigénique directe. Chez les lapins immunisés le pourcentage des neurones hypothalamiques sensibles est plus grand que chez les animaux natifs. La présence de petites quan tités de sérotonine au niveau des récepteurs péripheriques potentie l'action de l'endotoxine typhi murium.

PARTITION OF THE VERTICAL GRADIENT OF TRANSPULMONARY PRESSURE. E.D'Angelo, S.Michelini and E.Agostoni. Inst. of Human Physiology, Univ. of Ferrara, Ferrara, Italy.

Pleural surface pressure at various heights was measured after evisceration and diaphragm removal with closed airways and after change of the lung weight obtained by exsanguination (with intrathoracic extrapulmonary blood restored) or by placing tungsten beads in the airways. After diaphragm removal at constant lung weight the vertical gradient decreased by about 35 and 25% of the normal in supine and head-up rabbits, respectively. This gradient fraction, unrelated to gravity-independent shape effects, should be due to the gravity effect on the diaphragm-rib cage interaction. The gradient left over after diaphragm removal (25 and 15%, respectively) should be entirely due to the lung weight in the supine posture and nearly so in the head-up posture. The contribution of the lung weight to the vertical gradient computed in the supine posture by changing the lung weight agreed with that obtained through diaphragm removal experiments. The abdomen contribution to the vertical gradient was about 40 and 60% in supine and head-up rabbits, respectively, in line with previous findings.

THE INFLUENCE OF SOME EMPORAINE ORGANS ON THE UPTAKE OF MACROMOLECULES IN THE NEW BORN HAT INTESTINE. V.G. Daniels & R.N. Hardy. Physiological Laboratory, University of Cambridge, England.

The rat small intestine is known to absorb maternal antibodies and certain other macromolecules for up to 20 days after birth. Alternative mechanisms previously suggested for the abrupt change in permeability (closure) which occurs at this time include (a) alteration in diet at weaning, (b) enzyme development, and (c) replacement of immature mucosal epithelial cells. Factors (b) and (c) may be under the influence of the endocrine system. The process of closure in the newborn rat intestine in vivo has been studied by measurements of the uptake of 125I polyvinyl pyrrolidone (PVP). The effects of postnatal pinealectomy have been examined, since it is well known that prenatal pinealectomy results in histological changes in the epithelium of the foetal rat ileum. However, removal of the pineal gland in rats 2 - 8 days after birth had no effect on the subsequent uptake of PVP on days 16 or 22; closure occurred at the same time as in control animals. Injections of adrenal glucocorticoids are known to cause premature closure in young rats. The present experiments have shown in addition that removal of both adrenal glands 15 - 18 days after birth delays closure. This result suggests that the adrenal cortex has some influence on the uptake of large molecules, possibly through alteration of the circulating level of adrenal cortical hormones around the age of 18 days.

THE ACTIONS OF OUABAIN AND DIPHENYLHYDANTOIN ON SODIUM EFFLUX IN SINGLE BARNACLE MUSCLE FIBERS. B.G. Danielson, E.E. Bittar, S. Chen and E. Tong. Dept. of Physiology, University of Wisconsin, Madison, Wis., U.S.A.

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Sodium efflux in single muscle fibers from the barnacle Balanus nubilus is always exponential and reduced by K removal. The kinetic results based on the slope ratio of d/dt $\ln[Na^*]_i$ to d/dt $\ln(d[Na^*]_i/dt)$ indicate that in most fibers a fraction of the internal Na is sequestered. 10^{-4}M ouabain caused a 70% fall in Na efflux. This was almost twice as large as the effect of 10^{-4}M DPH. Application of DPH, followed by ouabain led to a 75% fall in efflux. Another difference in behavior of the pump toward these agents is that the onset of maximal inhibition with DPH is slower than with ouabain. A possible explanation is that the action of DPH on the Na-K-ATPase is incomplete or that DPH acts at a different site, e.g. the T-system. Raising the external K from 10 to 30 mM caused little stimulation of Na efflux. Inactivation of the ouabain-sensitive component with ouabain, followed by raising the external K to 30 mM led to a marked rise in Na loss. Experiments in which the external pH was lowered to 5.8 following inhibition of the pump with ouabain showed in every case a striking stimulation of Na efflux. Since acidification has a similar effect on Na efflux into K-free sea water in the absence of ouabain, the tentative conclusion is that acidification stimulates the Ussing mechanism.

URATE AND PAH TRANSPORT BY CHICKEN AND SNAKE KIDNEY SLICES AND ISOLATED PERFUSED SNAKE RENAL TUBULES. William H. Dantzler. Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724, U.S.A.

Previous work indicated that K⁺ is important for urate and PAH uptake by snake and chicken kidney slices. Depletion of tissue K⁺ reduced urate and PAH uptake. Uptake by chicken slices was restored in 5mM K⁺, but tissue K⁺ was only restored in 40mM K⁺, suggesting uptake is unrelated to tissue K⁺. K⁺ content of snake slices was restored in 3mM K⁺ but uptake was restored only in 40mM K⁺, indicating residual effect of K⁺ depletion on uptake. In present studies, K⁺-depleted chicken slices showed significant depression (over 30%) of heavy microsomal Na-K-ATPase activity. With incubation of these slices in media of increasing K⁺ concentration, recovery of enzyme activity paralleled recovery of tissue K⁺, suggesting lag in recovery of K⁺ may be related to enzyme activity. Incubation of snake kidney slices in K⁺-free medium had no residual effect on enzyme activity. This may be related to rapid recovery of K⁺ by these slices. Organic acid uptake was not related to enzyme activity. Several studies have been performed on transport of PAH by isolated perfused snake proximal tubules. These can be teased apart without use of enzymatic agents, held between glass micropipets in bath of bicarbonate buffered snake Ringer, and perfused with Ringer through glass micropipet for three to four hours. Addition of inulin to perfusion fluid showed no leakage. With 10⁻⁴ M PAH in bathing medium, PAH perfusion fluid/outside bathing medium ratio was only 0.7 at high perfusion rates (20-30 nl/min) but rose to about 2.7 at lower perfusion rates (5 nl/min), indicating active transport of PAH from bath to tubular lumen in this preparation. (NSF GB 11788).

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BLOCKADE OF AMNIOTIC FLUID INDUCED PULMONARY HYPERTENSION BY ASPIRIN AND OXYGEN.
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of Kentucky Medical Center, Lexington, Kentucky, U. S. A.

We have shown that bovine amniotic fluid given intravenously (0.05 to 3.0 ml) to young calves caused a biphasic rise in pulmonary arterial pressure. The early peak occurred within two minutes and the late peak, in 10 to 30 minutes. Examination of 14 bovine amniotic fluids showed that nine fluids caused the biphasic rise and five caused only the early rise in pulmonary arterial pressure. The early and the late rises were probably caused by two substances which were probably mucins. Pharmacological blockade with histamine, norepinephrine, and serotonin did not alter the biphasic pulmonary hypertension caused by amniotic fluid. However the pressure rises were prevented by oxygen breathing and by pretreatment with aspirin. The biphasic pulmonary hypertension and its blockade by aspirin suggested the mucin like substances in amniotic fluid were similar to rabbit aorta constricting factor releasing substance (RCS-RF) described by Piper and Vane, Nature, 1969. (Supported by National Institute of Health Grants HE 06780 and HE 08932).

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382 LABORATORY INDUCED ADVANCED HEAT ACCLIMATIZATION. Adolph R. Dasler. Naval Medical Research Institute, Natl. Naval Med. Ctr., Bethesda, Maryland, USA.

Heat acclimatization was studied in 92 volunteer test subjects classified according to: untrained-unacclimatized (A)(16 men), laboratory trained-acclimatized (B)(8), field trained-unacclimatized (C)(20), and field trained-acclimatized (D)(48). Type A, C and D subjects were tested twice, first in a cool environment (21 C DB, 15 C WB) and the next day in a hot humid environment (35 C DB, 31 C WB); air velocity was 0.5 m/sec. Each exposure was 110 min.; 50 min. work, 10 min. rest, 50 min. work. Metabolic rates at work were 180 KCal/m²-hr. Type B subjects underwent incremental physical conditioning for 10 consecutive days in the cool climate, immediately followed by 10 consecutive days of acclimatization in the hot-humid climate, with reexposure every 5 days for 9-10 weeks in the hot-humid climate. Type B men started their training at 150 KCal/m²-hr, progressing to 180 KCal/m²-hr by training day 7 and maintained at that level for all following exposures. Continuous recordings were made of 10 skin and 3 deep body temps., heart rate, respiratory min. vol., 02 consumption, ECG, and chamber temps.; intermittent recordings were made of blood pressures. Sweat rates were determined by weight loss. Chemical analyses were made of blood, urine, and sweat specimens. Findings from the classical parameters show the performance of type B men was equal to the best and better than the majority of type D men. Advanced heat acclimatization was successfully produced in the laboratory in untrained unacclimatized men. (Supported by U.S. Navy Bureau of Med. & Surgery Projects M4305.05-3028 and MF12.524.007-1002)

POSTGLOMERULAR REGULATION OF PROXIMAL FLUID REABSORPTION IN VOLUME EXPANDED RATS.

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U.S.A.

Studies were designed to delineate the precise contribution of changes in postglomerular vascular protein concentration (PVPC) to the depression in proximal reabsorption seen in rats during acute Ringer's loading (10% bw). Free-flow recollection micropuncture estimates of absolute (AR) and fractional (FR) proximal reabsorption, single nephron (SN) GFR and PVPC were obtained prior to and following volume expansion in 8 rats. Initial hydropenic values and percentage changes in these measures averaged 26.8nl/min±1.3SE(n=12) and -30% + 8(12), .60 + .03(12) and -49% + 5(12), 44.4n1/min + 1.8(12) and +35% + 5(12), and 9.5g% + 0.2(8) and -26.5% + 1(8), respectively. Using peritubular capillary microperfusion technics in these same volume expanded rats, we then determined the effects on AR and FR of selective restoration of PVPC to normal, pre-expansion levels with NaHCO3-Ringer's perfusate containing 9-10g% albumin. Despite continued volume expansion, and high and unchanged values for SNGFR (mean Δ =-4%) AR and FR rose by > 25% in 9/11 and 10/11 tubules, respectively, and on average were restored to within 80% of prior hydropenic values. As the methodologic control, microperfusion with 6-7g% albumin (a concentration equal to the measured PVPC in these Ringer's loaded rats) on average yielded no significant changes ((4%) in AR and FR. We conclude that the inhibition in AR following Ringer's loading is mediated predominantly by the resultant changes in PVPC. This inhibition in AR coupled with the measured increase in filtered load results in the observed depression in FR.

JUXTALEDULLARY FILTRATION RATE AND URINARY CONCENTRATING ABILITY. J.M. bavis and J.Schnermann, Inst. of Physiol. Univ. of Munich, W.-Germany

In addition to the effect of ADH on distal tubular water permeability, factors such as medullary blood flow or sodium delivery to the ascending limbs of the loops of Henle may participate in the concentrating process. We therefore measured filtration rates (N-GFR) of superficial (SN-GFR), middle (MN-GFR) and juxtamedullary (JN-GFR) nephrons during water diuresis (WD) and ADH-induced antidiuresis (AD) in rats with hereditary Diabetes insipidus, using de Rouffignac and Bonvalet's modification of Hanssen's FeCN-method. The following N-GFR (nl/min) were obtained during WD: SN-GFR 24,5 + 10,8 (n=103), MN-GFR 27,1 + 10,3 (n=100), JN-GFR 30,1 + 11,7 (n=100). During AD N-GFR (nl/min) were: SN-GFR 22,6 + 7,9 (n=92), MN-GFR 28,5 + 9,0 (n=96), JN-GFR 37,7 + 8,8 (n=91). N-GFR values in WD and AD differred significantly only for JN-GFR (p<0,005). The rise in JN-GFR after ADH is probably due to a rise in postglomerular juxtamedullary resistance to blood flow. This could be achieved either by a vasoconstrictor effect of ADH selectively on the juxtamedullary efferent arterioles or by an increase of the medullary blood viscosity. It is suggested that reduced washout of solutes and increased delivery of salt to the ascending limbs participate in determining the final urine concentration in ADH-induced AD.

De Rouffignac, and Bonvalet, J.P. Pflügers Arch. (1970) 315, 273-290.

EPINEPHRINE, NOREPINEPHRINE AND RENIN SECRETION IN THE NON-FILTERING KIDNEY MODEL. James
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A non-filtering kidney model without a functional macula densa was developed to study renin release (Blaine, E.H., J.O. Davis and R. Prewitt in Clin. Research 18:494, 1970). To prepare the model, the left ureter was ligated and the left kidney subjected to a 2 hour period of renal ischemia. On the third day after surgery, the right kidney was removed. On the fourth day, renin secretion by the left kidney was measured during a control period, during infusion of epinephrine (avg. rate of .45 μg/min) into the renal artery and during a recovery period. Renin secretion increased from 66 to 150 ng/min (P<.02) during epinephrine infusion and returned to 61 ng/min (P<.01) during the recovery period. In a second part of the experiment, the same dose of epinephrine was infused during the simultaneous infusion of papaverine (5 mg/min) into the renal artery; papaverine completely blocked the response to epinephrine. In a similar study intrarenal arterial infusion of norepinephrine (avg. rate of .9 μg/min) increased renin secretion from 156 to 340 ng/min (P<.05) and renin secretion returned to a recovery level of 125 ng/min (P<.05) but the response to norepinephrine was not blocked by papaverine. These findings suggest that epinephrine increased renin secretion through an action on the renal arteriolar smooth muscle whereas norepinephrine exerted its action, at least in part, by a direct action on the JG cells.

MECHANISM OF DIURESIS IN DCGS DURING BODY IMMERSION IN WATER. J. Terrance Davis and Arthur B. DuBois. Depts. of Physiology and Graduate Surgery, Univ. of Pennsylvania Sch. of Med., Philadelphia, Penna., U.S.A.

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Interest in the physiology of total body water immersion has been stimulated by a similarity to the state of weightlessness and by certain difficulties of fluid and electrolyte balance in the weightless state. A large diuresis uniformly occurs during immersion and has been attributed to redistribution of whole blood into the thorax and resultant stretching of the left atrial stretch receptors. However, data from our latoratory suggest that a peripheral rather than a central mechanism may be the more important cause of this diuresis. Direct measurement of left atrial transmural pressure in dogs revealed only small elevations. There were many individual diureses associated with no change or a fall in left atrial transmural pressure. There was no correlation (r=0.04) between the amount of left atrial pressure change and change in urine output. In addition, frequent serial determinations of plasma hematocrit, total solids, and osmolarity in nephrectomized dogs revealed prompt decreases in all of these shortly after immersion. This decrease would not be expected if whole blood were merely being shifted into the chest. It is suggested that the initial effect of immersion may be to change the pressures in the peripheral tissues at the level of the capillary in such a fashion as to cause movement of interstitial fluid into the vascular tree as theoretically predicted for the extremity by von Diringshofen in 1948 (Z. Kreislaufforsch. 37:382-390).

ROLE OF INTRAMURAL INNERVATION IN THE ACID RESPONSE TO GASTRIN IN DOGS. J.S. Davison & B. Schofield, Dept. of Physiology, Univ. of Bristol, England, and Medical Physiology, Univ. of Calgary, Calgary, Alberta.

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Acid secretion in vagally denervated gastric pouches in dogs is powerfully inhibited by small doses of atropine. An established hypothesis to explain this is that atropine suppresses tonic cholinergic potentiation of gastrin action on the parietal cell. Cholinergic agents are known to exert potentiation, and a local source could be the intramural plexuses. The ganglion blocking agent hexamethonium does not inhibit submaximal gastrin responses in these pouches in doses up to 4 mg/Kg iv which suppress motility. This implies that only the terminal elements of the neural chains could be concerned in the effect. The quarternary local anaesthetic lignocaine benzyl choloride applied topically in 3% solution to the mucosa of vagally innervated gastric pouches was shown to suppress secretory responses to vagus stimulation. Histamine responses were not reduced, suggesting that the drug penetrates to and exerts a specific effect on the terminations of the vagal pathway. A similar procedure did not reduce submaximal responses to gastrin in the denervated pouches. This failure, which is a further control of non-specific effects of the local anaesthetic, is strong evidence against any involvement of local neural elements in the acid stimulant action of gastrin.

1. Davison, J.S., Redford, Mary, and Schofield, B., J. Physiol. 195: 27P.

TIME COURSE OF MOTONEURON-PRESYNAPTIC INTERACTION IN THE CAT SPINAL CORD. E. E. Decima and R. Horn. Dept. of Anatomy, UCLA School of Medicine, Los Angeles, Calif. 90024, U.S.A.

The time course of motoneuron-presynaptic interaction was studied with a modification of Wall's technique for testing presynaptic excitability changes. The method used studied the firing probability of a group IA dorsal root fiber stimulated near its terminal endings on the motoneuron, by a micropipette inserted in the ventral horn of the cat spinal cord. The firing probability of a single presynaptic fiber was studied as a function of the time interval between the antidromic stimulation of motoneurons (the conditioning stimulus) and the cathodal pulse delivered near the presynaptic terminals by the micropipette (the test stimulus). The technique used showed that the interaction between post- and presynaptic elements can produce excitatory, inhibitory or both excitatory and inhibitory effects upon presynaptic terminals. The time course for this interaction varies for different presynaptic terminals, but in all cases the effects were synchronous with the recorded motoneurons antidromic field potential. These results are interpreted as indicating that via an electrical coupling, the motoneuron firing can depolarize, hyperpolarize or produce both effects upon the presynaptic boutons of dorsal root fibers making monosynaptic contact with the motoneuron somadendritic membrane. Supported by USPHS NB 07154.

CORRELATIONS BETWEEN SPLEEN AND CARDIAC FUNCTION. P.de Franciscis, G.Corsini, D.de Felice, G.Aufiero, A.Scapicchio, Inst. of Physiology-II Dept.-School of Medicine-University of Naples - Italy.

Experiments have been performed in animals in order to taste the effect of spleen on the heart. Splenic homogenate and subcellular fractions prepared from bovine spleen, with measurable protein content have been injected intravenously in intact dogs, in dogs with experimental myocardial infarction or with experimental heart failure. In other experiments isolated turtle heart has been perfused with spleen homogenate. Heart rate, ventricular blood pressure, peripheral or epicardial ECG, femoral blood flow and PO₂, PCO₂ and pH of arterial and coronary sinus blood content have been monitored. Our data indicated that no effect results from the injection of spleen homogenate in intact dogs, while animals with myocardial infarction show an immediate improovement of cardiac function: increase of sistolic ventricular pressure, decrease of diastolic pressure, rapid evolution of ischemic pattern of ECG, increase of peripheral blood flow, better utilization of O₂ from the heart. Dogs with experimental heart failure obtained by mean of beta blocking agents or ventricular preload show haemodinamic changes after spleen injection comparable with a digitalic effect of the homogenate. Perfusion of isolated turtle heart with splenic homogenate results in an increase of cardiac contractility.

390 SERUM PROLACTIN LEVELS IN PSEUDO PREGNANT RATS. R. P. Deis& Nia Alonso Inst. Investigación Médica, M. y M. Ferreyra, Córdoba. Argentina.

Rat serum prolactin as determined by radioimmunoassay during pseudopregnancy was found to be highest 6 hs and 12 hs after vaginal stimulation (VS) on oestrus day. On the 3rd day of pseudopregnancy serum prolactin levels was significantly higher in the afternoon than in the morning. The values obtained in the afternoon were similar to that obtained 6 hs and 12 hs after VS. A decline in serum prolactin was observed 8 hs, 24 hs, 3 days (morning), 10 days and 12 days after VS. Serum prolactin levels in pseudopreg nant rats, 10 min., 2 hs and 3 hs after VS were similar to that observed in normal oestrus rats. In a group of rats, serum prolactin was determined during the oestrus cycle. The highest value was observed in the afternoon of proestus and the lowest in procestrus morning and dioestrus 1.

NEOCORTICAL INTERFERENCE OF CARDIORESPIRATORY RESPONSES DUE TO SEPTAL STIMULATION. A.O.R.de Juan, E.T.Segura, S.D'Agostino and J.Negroni. Inst. Biomed.Engineer. and Inst.Biol.Med.Exp., Obligado 2490, Buenos Aires 28, Argentina.

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Experiments were done searching for an eventual interplay between neocortical and limbic influences upon autonomic functions in rats. Under urethane anesthesia the electrical stimulation of septal areas resulted systematically in an increase of the systolic blood-pressure, bradycardia, polypnea and changes in the ECG wave-form. Topical application of 3M KCl over the neo-cortex gave a similar picture excepting by hypertension which was absent. Partial or complete blockade of autonomic reactions was noted when septal stimulation was applied during neo-cortical depolarization. This efect does not depend on direct depolarization or on "spreading-depression" over the septum. On the other hand, a marked enhancement of responses after strychninization of the neo-cortex was observed. These results seem to suggest a close correlation between levels of neo-cortical excitability and septal discharges controlling cardiorespiratory mechanisms.

EFFECTS OF FRONTAL CORTEX LESIONS ON AVOIDANCE CONDITIONING IN MONKEYS.

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Nerveuse du C.N.R.S., Paris, France.

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The effects of Prefrontal (Pfr) and Premotor (Pm) lesions were compared in two situations: first, an avoidance-alimentary differentiation (AAD) in which, by pressing a bar during a signal, the monkeys could avoid a shock or obtain a food-pellet. Second, a delayed reaction (DR) test run according to the standard procedures in a Wisconsin General Test Apparatus. Confirming the classical data, the DR was drastically impaired by Pfr lesions, while it was left intact by Pm lesions. On the other hand, Pfr lesions produced no deficit in AAD, while Pm monkeys were significantly impaired in this test. In most cases, the avoidance response and the alimentary response were unequally affected by the Pm lesions.

THE PHYSIOLOGICAL ASPECT OF NUTRITION IN RATS WITH ETHYLIC CHRONIC PROGRESSIVE INTOXICATION. <u>Dr.E.de la Morena</u> and <u>Dr.H.J.Castro-Mendoza</u>.Inst. de Investigaciones Medicas,Fndn.Jimenez Diaz,Madrid(3),Spain.

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Previous experiences on experimental alcohol intoxication have been carried out mainly in adult rats in the acute (18 hours) and chronic (60 days) form. To 112 weaning albino rats of both sexes, 40-50 grs. in weight a commercial alcohol (brandy) was administered with the daily water drink. During the first 8 weeks the alcohol concentration was increased from 2.5% to 20%. This last concentration was further maintained for 24 weeks. A normal diet with 20% proteins and 10% fats was given throughout all the experiment both to the control- and to the alcoholic rats. Daily fluid intake ranged between 12-18 ml. Growth curve was followed weekly. The weight and size of the alcoholic rats were definitively less than those of the normals, being this difference bigger in males than in females. The "swimming test" is positive, and the EEG pattern strongly suggest cerebelous lesions. An increase in the NEFA content of plasma and organs was also observed. All these data indicate that probably the ethanol partially inhibits the growth hormone action upon protein and calcium metabolism.

PATHOGENESIS OF HYPERTENSION DERIVED FROM KIDNEY INFARCTION. I.J. de la Riva and Nidia 394 Basso. Centro de Investigaciones Cardiológicas, Universidad de Buenos Aires, ARGENTINA.

An increase in pressor responses to several vasoactive substances in rats with kidney infarction leading to hypertension has been observed by us. In the present study male Wistar rats (230g) were studied in order to determine if any electrolyte mechanism were involved. Bilateral kidney infarctions were obtained by the ligature of a branch of the renal artery. Two groups were analyzed: Group I (104 rats), at one week after the experimental procedure; Group II (49 rats), at three weeks after the experimental procedure. Electrolyte plasma concentration and total water and electrolyte contents in skeletal muscle and abdominal aorta (including all its branches) were analyzed. Blood pressure was directly recorded in the carotid artery. At one week, in the skeletal muscle, Cl and Na decreased similarly in both hypertensive and normotensive animals (P<0.05). Water and K content did not change. In the vessel wall, Cl decreased in hypertensive (6.0%) as well as in normotensive rats (10.8%, P<0.05) when compared with sham controls. Na did not change. Water increased in the infarcted rats (2.3%) when compared with sham controls (P<0.025). Hypertensive rats showed 9.3% more K than the normotensive rats (P<0.05). Plasma electrolytes were not modified. At three weeks, no significant changes were found. Thus K excess in the vessel wall was the only specific change in the hypertensive state at one week after the kidney infarction. If a comparable alteration occurs in the resistance vessels it could be related to the increased pressor responses observed during this period.

SEDATIVE EFFECTS OF HISTAMINE. B. DELBARRE, Neurophys. Lab., Faculté 395 des Sciences, 86 - Poitiers, France.

Histamine by I. M. or intraventricular route induced a loss of the righting reflex in chickens and prolonged the sleeping time induced by chloral hydrate in mice. The effects were dose dependent. The action with the chickens and with the mice were antagonized by previous treatment with adrenergic blocking drugs: dibenamine, phentolamine but not with phenoxybenzamine. In mice but not with chickens, atropine is a strong antagonist. In chicken, sedative effect of histamine is potentiated by cyclic AMP (DB-AMP). EEG and EMG tracings were collected. Histamine does not induce paradoxal sleep. The antiavoidance activity of histamine in rat trained in a shuttle box or skinner box (sidman avoidance procedure) was found to be significantly reduced when administered with a concurrent dose of atropine but not with methylnitrate atropine. These results suggest the possibility that histamine plays a role

CHANGES IN HEART RATE AND POTASSIUM BALANCE IN ISOLATED RAT HEART. 396 M.F. de Lew, A.O. Grassi, H.E. Cingolani. Institute of Physiology. School of Medicine. University of La Plata. Argentine.

The positive inotronic response to increases in heart rate, "staircase" phenomenon, is the usual in most mammalian species and a simultaneous potassium loss has been described (Sernoff S.et al., Amer. J. Med. 34, 440, 1963) An increase in frequency of contraction leads, however, to a decrease in contractility in the rat myocardium. It was considered then of interest to study in this specie the myocardial potassium balance that follows changes in rate.

Rat hearts were perfused with Ringer solutions at 37°C; the frequency was controled by means of an elctronic stimulator. Contractility was

assessed by apex to base amount of shortening and its velocity.

The increase in rate from 100 to 200 beat/min produced a potassium loss of 1.28 ± 0.36 µEq/gr.(P<0.01).Contractility showed a previous increase followed by a decrease to lower levels than control. The increase in contractility was observed during 50 sec., while the potassium loss was statistically significant during 5 min.

RELATION OF PALLIDAL AND PUTAMEN NEURONS TO LEARNED MOVEMENTS. M. DeLong, National Institute of Mental Health, Bethesda, Maryland, USA.

Activity of neurons in the putamen and globus pallidus was recorded in awake monkeys during learned movements of the extremities. In animals trained to perform rapidly alternating movements with either arm, it was found that, of units related to these movements, the majority were best related to the contralateral arm; these were located in the lateral portions of both the internal and external pallidal segments and the putamen. When the rapidly alternating movement was performed with either arm or leg, units related to arm movement typically showed no relation to leg movement and visa versa. Units related to the leg were also located within the lateral portions of the two pallidal segments. In order to determine the timing of the discharge in relation to the onset of movement, animals were trained to grasp an immovable rod and steadily push or pull and then rapidly reverse the direction of the force at the presentation of a visual stimulus. Units in the contralateral putamen and globus pallidus were studied during repeated (>50) trials. Numerous units in both nuclei exhibited distinct changes in activity prior to the onset of movement. Related units often showed distinctly different levels of activity during maintained pushing and pulling and in relation to the transient shift between the two steady states. These observations provide evidence for localization of function within the basal ganglia and for a role of these structures in the initiation of movement. The output from the pallidum to the precentral cortex (via thalamus) may influence the motor cortex prior to the onset of

EFFECT OF PERITUBULAR PERFUSION ON H ION SECRETION IN FROXIMAL TUBULES OF RAT KIDNEY. Margarida de Mello Aires and Gerhard Malnic. Dept. of Physiology, Univ. of São Paulo, São Paulo, Brazil.

The rate of II ion secretion by rat proximal tubules was evaluated during microperfusion with isotonic solutions containing 100 mEq/1 NaICO3 or 95 mM/1 Na2HFO4 and raffinose, recording pH changes by means of an antimony microelectrode. After several control perfusions, the peritubular capillaries of the studied tubule were perfused with solutions of variable composition. During this perfusion the measurements of II ion secretion rate were repeated. Capillary perfusion with mammalian bicarbonate Ringer's containing acetate and preequilibrated with 5% CO2, for periods of up to 6 minutes, did not change significantly the rate of tubular acidification as well as the level of steady-state pII. The use of air equilibrated bicarbona te Ringer's at a pH of 8 led to more alkaline steady-state pH levels. Perfusion with phosphate Ringer's at a pH of 7.37 equilibrated with air did not change significantly the II ion secretory rate. Addition of 10-3 N ouabain to peritubular perfusion fluid reduced the rate of acidification by 27%. These findings indicate that peritubular perfusion during relatively short periods with artificial solutions preequilibrated with CO2, and even at low pCO2 but at a physiological pH, can maintain near normal tubular acidification, and that this process is impaired by ouabain.

ON THE ROLE OF CALCIUM AND EXOGENOUS CYCLIC 3', 5' AMP IN CONTRACTILE RESPONSE INDUCED BY NORADRENALINE IN ISOLATED RAT AORTA. F. DEMESY and J.C. STOCLET. Lab. Pharmacodyn., Fac. Pharm., Univ. L. Pasteur, Strasbourg, France.

There is increasing evidence that cyclic 3', 5' AMP participates with calcium in the control of vascular tone and contractility, but the mechanism of this control is still unknown. The influence of exogenous N-2'-0-dibutyryl-adenosine-3', 5'-monophosphate on the "spike" and "tonic" phases of the isometric response of rat aortic strips to noradrenaline is studied in different extracellular fluid calcium concentrations. Cyclic AMP at low concentrations (0.1 up to 0.2 μ M) gradually inhibits both phases of noradrenaline induced contraction. The tonic phase partially persists but decreases after a while and rythmic activity appears. Raising extracellular calcium concentration up to 10 mM during the partially persisting tonic phase rapidly abolishes the tonic phase and rythmic activity. Cyclic AMP at higher concentration (1.5 μ M) induces a short increase of aortic tension. The influence of cyclic AMP on vascular fibres calcium movements and storage and the consequences on excitation-contraction coupling are discussed.

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400 CONCERNING THE FUNCTIONS OF THE BIRD PECTEN.G.G. Demirchoglian.Lab. of Visual Reception of the Acad. of Sciences of Armenian SSR, Erevan, USSR.

To study the functional role of the pecten in the bird's eye, electroretinographical investigations have been carried out by perimetrical stimulation of various areas of the retina. The decrease of ERG response has
been established during illumination (also of sunlight) in the area of the
pecten with simultaneous intensification of rapid photoresponses, of the
type of early receptor potential, arising before the appearance of a wave
ERG. The study of spectral characteristics of the isolated pigeon pecten
has revealed an intensive absorption of blue light when the red light
passes. But the pecten as a biological filter with selective absorption
shows a change of spectral characteristics after intensive irradiation.
Experiments have also been performed showing the change of retinal photoresponse when birds were placed in a magnetic field. This phenomena can be
explained as photomagnetic concentrational effect. On the basis of the
well known data on the sum-compass orientation of birds and the investigations performed, a hypothesis (G.G.Demirchoglian 1966, 1968) has been developed concerning the pecten as a biological reconstructing light filter
and a photomagnetic receptor.

POST NATAL CHANGES IN THE VAGUS EFFECT ON THE HEART RATE. K.J.de Neef, A. Versprille and M.E. Wise. Clinical Physiological Lab., Departments of Pediatrics, Obstetrics and Physiology, University of Leiden, The Netherlands.

The quantitative relation between vagal stimulation and lengthening of the heart interval is described as $I_f=I_0L^f$, in which I_f is the heart interval during stimulation, I_0 before stimulation, L is the lenthening factor for a particular vagal nerve and f the number of vagal stimuli per second. Alternatively $I_f=I_0e^{fb}$, where $b=2.3026\,\log_{10}L$. Estimates of $\log_{10}L$ (=H) have been obtained as the mean of $\{\log_{10}(I_f/I_0)\}/f$. The values of H in neonatal rabbits are about 3 times those in rabbits a few weeks old. In a second series with physostigmine H was found to increase by about the same ratio in both groups. This means that in neonatal rabbits AChE is active and not responsible for a lower vagus activity in older animals. In a third series animals of both age groups were treated with reserpine. This brought the H values of the older group into the range of the neonatal group for which H was not increased. These results suggest that catecholamines developing in the first week of post natal life counteract the vagus effect on the heart rate. (Supported by ZWO/FUNGO).

THE KIDNEY IN Ca HOMEOSTASIS: MECHANISMS CONTROLLING Ca EXCRETION DURING PHOSPHATE DEPLETION. G. Denis and A.V. Kuczerpa. Dépt de Physiologie, Université de Montréal, Montreal, Quebec, Canada.

Ca excretion and reabsorption was studied in normal and thyroparathyroidectomized (TPTX) rats fed diets containing 0.02% P & 0.05% Ca and, 0.4% of both with 3.3, 11 and 33% protein. A logarithmic depression of plasma P occurred with increasing levels of dietary protein in the former and arithmetic in the latter group. Diet deficient in P and Ca, high in protein, produced functional parathyroidectomy. Diets low in protein did not. Increased filtered loads with increasing dietary protein could not account for the increased Ca excretion in the rats on low Ca and P diets but did in rats fed 0.4% of both. In the rats fed P and Ca dedicient diets with 33% protein, plasma P and Ca excretions were of the same magnitude in normal and previously TPTX rats while, plasma Ca was much lower in the latter group. After nephrectomy plasma Ca increased at the same rate for the first two hours in TPTX and normal rats which had been fed P and Ca deficient diets with 33% protein. Hypercalcemia became more marked in the TPTX rats four hours after nephrectomy when plasma P began to rise. These studies suggest that the kidneys, not calcitonin control hypercalcemia when plasma P is depressed and, that Ca reabsorption is dependent on both parathormone and plasma phorphorus.

THE VASCULAR ACTION OF CORTICOTROPING RELATION TO THE MORK CAPACITY. P. Derevenco, Vera Derevenco, Lucia Racoviță, I. Imreh. Inst. for Public Health and Med. Res. Dept. of Nuclear Med. Cluj, Romania

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The action of corticotropine(C) on the blood flow of hypophysis, adrenals, thyroid, liver, kidney, myocardium and striated muscle, measured by a variant of the rubidium-86 method(Sapirstein) is studied in rats. The synthetic C(Synacthen Ciba) injected i.v.(lo,50,or 200 mU/loo g body weight) produces a rapid increases of the adrenal blood flow, in direct proportion with the dosis. The lyophilised C(Cortrophine Endo) acts similarly. In the other organs it prevails after the littlest dosis a vaso-constriction and after the greatest dosis a vasodilatation. C with prolonged action(Synacthen R Ciba or Cortrophine Z Organon)(800 mU/loo g x 5 i.p.injections) produces in rest a significant vasodilatation in adrenals and kidneys. After swimming(lh) the hormone leads to a significant rise of the blood flow in adrenals, hypophysis and liver. The vascular action of C, which has probably a extraadrenal mechanism, could explain the relative vasodilatation of the trained animals and also the increase of the work capacity observed after C in other experiments.

EFFECTS OF STIMULATIONS AND LESIONS OF MONOAMINE NEURONAL SYSTEMS ON SLEEP AND WAKEFULNESS IN MONKEY. T. Destrain. Dept. of Physiology, All India Institute of Medical Sciences, New Delhi-16, India.

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Electroencephalogram (EEG), electrooculogram (EOG) and neck nuchal electromyogram (EMG) were recorded during sleep and wakefulness in twelve rhesus monkeys carrying chronically implanted bipolar electrodes. EEG patterns of dorsal and ventral raphe nuclei which contain 5-HT neurons and of adjacent dorso-lateral reticular areas which contain NA neurons (A6 and A7) were more desynchronized than of cortical areas during sleep. Low frequency (5 to 10/sec) stimulations of the two monoamine systems could occasionally facilitate occurrence of high voltage slow-wave sleep (SS) and seldom low voltage fast-wave sleep (FS). Electrolytic lesions of raphe caused reduction in amplitude of EEG synchronization during SS and also instability in onset. Lesions of dorso-lateral areas caused no marked effect on sleep or EEG. When both raphe and dorso-lateral areas were lesioned typical SS and FS were abolished and only short episodes of sleep with poorly synchronized EEG were present. Such episodes could not be characterised as any of the known stages of SS or FS. This dissociation between sleep behavior and EEG characteristics decreased progressively in four weeks when some FS could be differentiated from SS. The data show that 5-HT and NA systems together play important controls in sleep function.

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REGURGITATION OF SULFONAMIDES DURING CHOLESTASIS. A. Despopoulos, P.C. Hirom, P. Millburn and R.T. Williams. St. Mary's Hospital Medical School, London W. 2, England.

In hepatic portal triads, blood and bile flow in opposite directions suggesting that counter-current exchange could contribute to regurgitation of solutes from bile. Seven sulphonamides which in vitro are concentrated in bile by a probenecid sensitive process were injected retrogradely into bile ducts of female rats. Dose was 0.5 micromol in 0.1 ml saline solution. Contact time was 2 min at 20 cm water occlusion pressure. After release of occlusion, most of the drug recovered in the bile was present there within 5 min; after 30 min excretion of drug was negligible. 50 - 90% of drug was lost from the bile ducts, substantial amounts appearing in the urine. Similar data were obtained in isolated perfused rat livers. In the latter preparation, drug could be detected in effluent blood within 1 min within release of biliary stasis. These data indicate that large amounts of drugs can escape biliary excretion by recycling between bile ducts and afferent hepatic blood. Current concepts of enterohepatic circulation should be extended to include this possibility.

LOCALIZATION AND ACTIVITY OF CHOLINESTERASE (CHE), CHOLINACETYLASE (CHA) AND ACETYLCHOLINE (ACH) IN MUSCLE FIBERS AND MOTOR AXONS OF LOBSTER WALKING LEG NERVE. W-D. Dettbarn 1, Med. Sch., Vanderbilt University, Nashville, Tenn., U.S.A., A.J.D. DeLorenzo 2, Med. Sch., Johns Hopkins Univ., Baltimore, Md., U.S.A., and M. Brzin 1, Med. Sch., Univ. Ljubljana, Ljubljana, Yugoslavia.

Cholinergic compounds which act specifically on neuro-muscular preparations of vertebrates, effect the lobster preparation only when applied in high concentrations. Electron-microscopic cytochemistry and microgasometric measurements of CHE in isolated excitatory and inhibitory fibers revealed no differences either in localization or in the rate of hydrolysis, regardless of the specific function of the axon. No cytochemical reaction indicating CHE activity was found in the synaptic region proper. In the muscle fibers ChE was limited to the transverse tubules at the dyads and occasionally in cisternae of the sarcoplasmic reticulum. No activity was observed in the tubules outside the region of the dyads or close to the contractile elements of the muscle fiber. CHA activity was highest in the axons, with no apparent distinction between the two types investigated. The terminals showed a significant reduction in activity when compared to more proximal parts of the axons. Axon free muscle showed a still lower CHA activity than the nerve terminal. The even distribution of CHE, and CHA in excitatory and inhibitory axons, in contrast to the specific distribution of Glutamate and Gaba, points to a more general role of the ACH-system in the metabolism and function of these fibers. Supported by U.S.P.H.S. Health Sciences Advancement Award #5 SO4 FR 06067-03.

TRANSFER OF MONOVALENT ANIONS ACROSS THE RED CELL MEMBRANE. B. Deuticke. Dept. Physiol., Med. Faculty, Techn. Univ., Aachen, Germany

The transfer of monovalent inorganic and organic anions (SCN-, NO $_3$, α -hydroxy-carboxylates,e.g.lactate; α -keto-carboxylates,e.g.pyruvate)across the red cell membrane was studied by measuring their net exchange with cellular Cl- in ox red cells. Variation of temperature as well as inhibitors were used in order to obtain penetration rates measurable by conventional methods of cell/medium separation. SCN- and NO $_3$ exchange with Cl- at rates(min-1) of 0.475 and 0.741,respectively(0°C,pH 7.9, Hct 45%). The transfer of α -hydroxy-carboxylates(1-8 C atoms) proceeds much slower. Rate constants(10°C, pH 7.5, Hct 45%) are highest for glycolate(0.123),low for lactate(0.004) and then increase with the number of C atoms. In contrast, the activation energies(kcal/mole)of the exchange diminish progressively from glycolate(28.6) to α -hydroxy-octanate(15.2). The transfer of monovalent anions is inhibited by amphiphilic compounds(e.g.fatty acids,tetracaine,salicylate(1-5 mM)),previously shown to reduce the transfer of divalent anions. In case of the organic monovalent anions,however, the inhibition disappears when their chain length exceeds 3-4 C atoms. The results support the view that non-ionic as well as ionic interactions with membrane components are involved in the process of anion transfer in the red cell. Supported by the Deutsche Forschungsgemeinschaft(De 168).

BEHAVIORAL EFFECT OF DESGLYCINAMIDE LYSINE VASOPRESSIN (des-LVP), A RECENT-LY ISOLATED PEPTIDE FROM HOG PITUITARIES. D. de Wied, A. Witter, S. Lande, H.M. Greven. Rudolf Magnus Inst. for Pharmacology, Med. Faculty, Univ. of Utrecht, The Netherlands.

Lysine vasopressin (LVP) facilitates the consolidation of active avoidance behavior. A single subcutaneous injection of 60 mU at a critical period of time after completion of avoidance learning, inhibits extinction of a pole jumping avoidance response for at least 2 weeks, while saline treated rats extinguish in 2-3 days. Desglycinamide lysine vasopressin (des-LVP) which was recently isolated from hog pituitaries appeared to exhibit a similar action. A single injection of 0.5 μg des-LVP inhibits extinction of a pole jumping avoidance response to the same extent as 60 mU LVP. The pressor-, antidiuretic-, oxytocic-, and CRF-activity of des-LVP, however, is less than 1% of that of LVP.

MECHANISM OF INCREASE IN ARTERIAL BLOOD PRESSURE DURING STATIC EXERCISE. P. B. Dews and J. A. Herd. Harvard Med. Sch., Boston, Mass. 02115, U.S.A.

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During strong sustained contraction of skeletal muscles in intact subjects there is an increase in arterial blood pressure (and heart rate). The increase occurs, for example, during a strong hand grip. It has been supposed that the increase in blood pressure results, at least in part, from nervous influences transmitted over efferent autonomic pathways. We have trained Rhesus monkeys to pull a T-bar with a force in the range of the total body weight of the animal. Blood pressure was measured through a tube permanently inserted into the lower descending aorta via the internal iliac artery. Pulling the bar was accompanied by an increase in arterial blood pressure. When increasing doses of hexamethonium were administered, the resting blood pressure was lowered, but the increment during pulling was not abolished. Indeed the increment was greater rather than less than before hexamethonium. We have now shown that the increment is not reduced by phentolamine. It therefore appears that a substantial contribution to the increase in blood pressure during effort is mediated by mechanisms not requiring a functional autonomic nervous system.

FAILURE AND RECOVERY OF HEARTS AFTER PERFUSION WITH Ca++-FREE MEDIUM. N.S. Dhalla and J.C. Yates. Dept. of Physiol., Fac. of Med., Univ. of Manitoba, Winnipeg, Canada.

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When isolated rat hearts were perfused with Ca++-free medium, both contractile force and dF/dt declined to zero within 30 sec. The onset of failure was associated with a decrease in time to peak tension and an increase in time to 1/2 relaxation. No changes in ultrastructure or high energy phosphate stores of the myocardium were apparent within 3 min of perfusion with Ca⁺⁺-free medium. Separation of intercalated discs was noted in hearts perfused for 10 min with Ca⁺⁺-free medium and also in hearts perfused with normal medium containing 1.25 mM Ca⁺⁺ following perfusion with Ca⁺⁺-free medium for 3 min. The resting tension increased during perfusion with Ca⁺⁺-free medium; a further dramatic increase in resting tension was observed when the hearts preperfused for more than 3 min with Ca⁺⁺-free medium were switched to the normal medium. The changes in electrical activity which occurred after the onset of failure were irreversible 3 to 4 min after perfusion with Ca++-free medium. The contractile force did not recover in hearts perfused for 4 min with Ca++-free medium. The failure due to Ca++-free medium was delayed and the recovery was augmented by lowering the concentration of Na⁺ in the perfusion medium whereas changes in the concentration of K⁺ or Mg⁺⁺ had no effect. The results reveal a defect in excitation-contraction coupling in hearts perfused with Ca⁺⁺-free medium and it appears that extracellular Na⁺ plays a deleterious role during failure and recovery of these hearts. (Supported by Medical Research Council of Canada and Manitoba Heart Foundation.)

EVIDENCE FOR A TRANSMITTER ROLE OF GLYCINE IN CAT SPINAL CORD. B.N.Dhawan, J.N. Sharma and R.C. Srimal. Ctr. Drug Res. Inst., Lucknow, U.P., India.

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Intrathecal injection (i.t.) of glycine (2.5 to 5.0 mg) produces almost 100% inhibition of flexor (FR) and crossed extensor reflex (CER) in chloralosed cats. It fails to affect the patellar reflex (PR) and its polysynaptic facilitation and inhibition even in large doses. Linguomandibular reflex (LMR) is inhibited by intraventricular (i.c.v.) administration of 10-20 mg glycine. The pressor responses to electrical stimulation of the medullary vasomotor center are not inhibited. Facilitation of FR, CER and LMR by i.t. or i.c.v. strychnine sulphate (10-20 µg) is also antagonised by the same or slightly higher dose of glycine. GABA has been tested similarly and found to be 5-6 times less active at spinal level but equiactive at medullary level. It has been a much weaker antagonist of strychnine. The results support the possibility of glycine acting as an inhibitory transmitter in the spinal cord.

A COMPARISON OF THE RESPIRATORY FUNCTIONS OF BLOOD OF ASIAN AND AFRICAN ELEPHANTS.

D. S. Dhindsa, C. J. Sedgwick and J. Metcalfe. Heart Research Laboratory, Univ. of Oregon Med. Sch., Portland, Oreg., and San Diego Zoo, San Diego, California, USA.

The respiratory characteristics of whole blood from 4 female Asian elephants (Elephas

The respiratory characteristics of whole blood from 4 female Asian elephants (Elephas maximus) and 3 female African elephants (Loxodonta africana africana) were studied. Each elephant was immobilized with M99 (a morphine derivative), and blood was withdrawn from an ear vein. Oxygen dissociation curves of whole blood were constructed at 37°C and were corrected to a plasma pH of 7.40. The mean blood P_{50} values were 25.2 \pm 0.5 and 23.2 \pm 1.3 mm Hg for Asian and African elephants, respectively. The oxygen affinity of Asian elephant blood was significantly lower (p<.01) than the oxygen affinity of blood from African elephants. The Bohr factor (mean = -0.351 \pm 0.029, n = 35) and the Haldane effect were similar for both species. The blood morphology was similar in the two species, but the leukocyte count was significantly higher in Asian elephants. Starch gel electrophoresis showed that the hemoglobin of Asian elephants traveled at a slower rate than the hemoglobin of African elephants. Blood drawn anaerobically from an ear artery of one Asian elephant had a P_{02} of 72.2 mm Hg at pH 7.439; corrected to pH 7.40 this gave a hemoglobin saturation of 98%. This study was supported by the Oregon Heart Association and PHS Training Grant #HE-05499 and Research Grant #HE-06042 from the National Heart Institute.

413 EFFECT OF MIRACULIN ON HUMAN TASTE BUDS. H. Diamant and Y. Zotterman. Ear Clinic, Umeå and Dept. of Physiology, Veterinärhögskolan, Stockholm, Sweden.

Extracts of the fruits of Synsepalum dulcificum containing a glycoprotein generally called Miraculin has been known to add a sweet component to the taste of acid drinks. As this effect is limited to humans, the summated electrical response from the chorda tympani has been recorded during middle ear surgery before and after the application on the tongue of Miraculin and a subsequent application of extracts of Gymnema silvestris. After Miraculin the response to citric acid was found to be augmented. Brushing the tongue with Gymnema, which abolishes the sweet taste, brought down the response to citric acid to the previous value. These results indicate that under the influence of Miraculin acids stimulate a certain number of "sweet fibres".

414 EARLY MALNUTRITION, BRAIN GLYCOPROTEINS AND BEHAVIOUR IN RATS.

C. Di Benedetta and L. A. Cioffi. Institute of Human Physiology, University of Naples, Italy.

Different nutritional levels were induced by varying the number of rats in the litters and by feeding diets of different protein concentration at weaning for four weeks. Rats with different nutritional levels during the suckling period and at weaning show significant changes in the body as well as brain, heart, and liver weight. The slight, though significant, decrease of the brain weight is interpreted in terms of less content of labile tissue.

The acrylamide gel electrophoresis of brain soluble proteins and glycoproteins shows lesser degree of heterogeneization in the undernourished animals.

The exploratory behaviour is slightly affected by the different nutrition histories. The avoidance conditioning, measured by means of a shuttle-box, is appreciably affected by the different nutritional levels in the suckling period and by undernutrition after the weaning.

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EFFECT OF CERTAIN ENZYMES ON THE ULTRASTRUCTURE OF SYNAPSES. Vincenzo Di Carlo. Dept. of Anatomy, Loyola Univ. of Chicago, Stritch Sch. of Med., Maywood, Ill. 60153 and L. B. Mendel Res. Lab., Elgin State Hosp., Elgin, Ill.

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Incubation at the appropriate temperature of amphibian or mammalian brain cortex slices in oxygenated Ringer solutions with or without addition of certain drugs or enzymes allows one to study by electron microscopy the ultrastructural changes produced by such treatments. By careful manipulation of the slices, good preservation of the tissue can be obtained in the control preparations. We utilized such a technique in order to acquire information about the chemical nature of certain components of synapses in cerebral cortex. In brief, a 15-min. incubation in 0.1% trypsin appeared to cause digestion of synaptic filaments and postsynaptic thickenings. These structures, on the other hand, were apparently unaltered after treatment with even higher concentrations of RNase, DNase or neuraminidase. Incubation in DNase seemed to increase the amount of electron-dense material in between synaptic vesicles and in the immediate vicinity of the presynaptic membrane. Incubation in neuraminidase appeared to induce a decrease of extracellular space (the opposite happens with the other enzymes) and widespread fusion of the plasma membranes of adjacent cells.

STATE OF INTRACELLULAR SODIUM IN AMPHIBIAN COCYTES. D.A.T.Dick and D.J.Fry. Dept. of Anatomy, University of Dundee, Dundee, Scotland.

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Current theories of the state of intracellular Na tend to assume either that it is free or that it is bound. Although all Na in the oocyte appears to be free since it is replaceable by external radioactive Na, three types of evidence suggest that some of it is not readily replaceable by external Li. (In all radioactive experiments occytes were loaded for 10 - 12 hours in Ringer solution containing 22NaCl.) (1) 22Na efflux into Li Ringer solution ceases when some intracellular 22Na still remains. (2) In Ringer solution the Na activity/concentration ratio measured by a glass microelectrode is only 50% of that in free solution, and only 8 - 14% in an occyte exposed for 5 hours to Li Ringer solution. (3) Autoradiography in frozen sections of occytes exposed to Li Ringer solutions shows that the cytoplasmic ²²Na concentration is 2.2 times that in the nucleus. The Na component which exchanges slowly or not at all with Li thus appears to lie in the cytoplasm. It is not retained by a dialysis membrane after cell rupture, so it is more likely to be held in some membranous component than bound to This Na fraction has been designated as 'sequestered' rather than 'bound'.

ANION AND INERT GAS CLEARANCE FROM THE SYNOVIAL CAVITY. W. C. Dick, Univ. Dept. of Med., Glasgow, Scotland. S. Deodhar and W. W. Buchanan.

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The rate of clearance of 133Xenon from the joint cavity provides an indirect measure of synovial tissue perfusion (1) and may be employed to detect pharmacologically induced changes in the synovial perfusion rate (2). In the present study the results of animal experiments in which over 90% of intra-articularly injected 133Xe could be recovered in the femoral vein will be presented to establish that clearance of the inert radionuclide is mediated by the venous system. The simultaneous clear ance rates of 133Xe and of either ^{131}I or ^{99}mTc were monitored and the The simultaneous clearrespective anion was found to clear faster from the joint cavity than the inert gas. When KC104 was administered beforehand however the anions cleared more slowly than 133Xe suggesting the presence of an anion transport mechanism from the synovial joint cavity.

(1) Dick, W. C., St. Onge, R. A., Gillespie, F. C., Downie, W. W., G., Gordon, I., Whaley, K., Boyle, J. A. and Buchanan, W. W. (1970). Ann. Rheum. Dis., 29, 131-134.

(2) Dick, W. C., Provan, C. and Pond, M. Res. Vet. Sci. (in press).

THE RENAL HANDLING OF SODIUM AND WATER LOADS, STUDIED ON A DIGITAL COMPUTER MODEL OF THE SYSTEMIC CIRCULATION AND KIDNEY. C.J.Dickinson. Medical Unit, Col.Hosp.Med.Sch., London, England.

A digital computer model has been made to study highly complex physiological interactions occurring over hours or days. It has been given a human-size systemic circulation, with blood, interstitial fluid and cellular compartments, baroreceptor reflexes controlling arterial resistance, venous capacitance and cardiac contractility, vasopressin, aldosterone, angiotensin and erythropoietin, with the best available estimates of the speed of movement of water and ions across cell and capillary membranes, and into the urine. The model contains only known physiological systems. Experiments with this model show: 1) after adrenalectomy the excretion of an acute water load is considerably delayed; 2) when hypertension is allowed to develop and stabilize, a few simulated weeks after renal artery constriction, the model exhibits an accelerated rate of excretion of a saline load; 3) in the presence of simulated primary hyperaldosteronism there is polyuria and polydipsia. I conclude that physiological information already available is sufficient to explain a number of wellknown physiological and clinical observations, without the necessity for invoking new mechamisms.

THE EFFECT OF OUABAIN ON POTASSIUM EFFLUX IN MYELINATED NERVE OF FROG. F.P.J. Diecke. Dept. of Physiology and Biophysics, University of Iowa, Iowa City, Iowa, U.S.A.

A component of potassium efflux which is modified by ouabain has been investigated in myelinated nerve of frog. Upon application of ouabain (10-4M) potassium efflux in resting nerves increases by 30-40%. It has been demonstrated that during the increased potassium efflux the membrane potential and membrane conductance remain constant. The increased flux due to ouabain, therefore, appears to be independent of the passive permeability of the membrane. The "ouabain-modified" potassium efflux is significantly affected by the external sodium and potassium concentrations. Increasing the external sodium concentration from 0 to 115 mM activates the "ouabain-modified" potassium efflux with 50% activation at 15 mM. Increasing extracellular potassium concentrations also activates this efflux component. The experimental results can be compared to kinetic models of carrier-mediated transport. Supported by USPHS Grant NS-05188.

C N V AS A CRITERION OF ASPECTS OF MENTAL CAPACITY. E.G. Dincheva, E. Atzev, D. Popivanov. Inst. of Labour Protection and Occupational Diseases, Department of Work Physiology, Sofia, Bulgaria.

15 men and women aged from 18 to 30 years were examined. The classical paradigm of CNV was complicated by additional insertation of the electric stimulation - S_3 among S_4 and S_2 . The addition stimulation in pseudooccasional order, does not submit or submits in three different spots after S_4 . It has been established a different possibility for the various people to remember the time for coming of S_3 , which is connected with the appearance of CNV. The possibility of memoring the time of the approaching of the additional stimulation is proposed as a method for measuring of some aspects of the mental working capacity.

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THE EFFECT OF PH ON THE CHLORIDE FLUXES OF A SINGLE BARNACLE MUSCLE FIBER. R.DiPolo and F.J.Brinley, Jr., Dept. Physiology, Johns Hopkins Univ. School of Medicine. U.S.A. Cannulated single muscle fibers were dialysed with a porous capillary. Membrane potentials were recorded with a second longitudinally-inserted glass capillary filled with 0.5 M KCl. The basic internal medium contained (mM): K-Isethionate, 170 or 190, KCl, 30 or 5; Na-TES, 15, Tris-EGTA 10; MgSO₄, 4; Sucrose, 550; pH: 7.0. The external medium contained (mM): NaCl, 465; KCl, 10, CaCl₂, 25, MgCl₂, 8; Na-TES, 2, pH: 7.5. Temperature: 23-25° C. pH buffers were Tris-HPhthalate (pH: 3.9-5.0), Tris-Cl (pH: 8.9-9.1). The resting chloride efflux was found to be 140±24 (n=12), and 18±5 p-mole/cm².sec (n=31) for an internal chloride concentration of 30 and 5 mM respectively. Changes in external or internal pH were found to affect the chloride efflux in the following way: a) pH: 3.9, an increase in the efflux was observed for external and internal changes in pH, although the effect was transitory for external pH changes b) pH: 5.0, a 40 to 50% decrease in the efflux was observed for external pH change. A similar increase in the efflux to that observed at pH 3.9 was found for internal pH change. c) pH: 9.0, a 10 to 20% increase in the efflux was found upon changing the external pH. A marked increase in the chloride influx was found at external pH of 3.9. These experiments indicate: 1) the presence of a sharp increase in the chloride fluxes at pH below 5.0. and 2) a different behavior of the efflux at pH 5.0 with respect to internal and external pH changes.

SPECIFICITY OF HORMONAL REGULATION OF SODIUM TRANSPORT IN NEPHRONS OF YOUNG RATS. H.Dlouhá, K. Čapek. Inst. of Physiology, Czechoslovak Academy of Sciences, Prague, CSSR.

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Developmental changes in hormonal regulation of sodium transport and water movement have previously been observed in the kidney during ontogeny. Rats aged approximatly 22 days are more sensitive to the antidiuratic action of vasopressin than older animals. In the younger age group vasopressin has a more marked natriuratic action. The influence of aldosterone on the kidney is alsayage dependent. In micropuncture studies TF/P values for ¹⁴C Inulin, ²Na and potassium were measured in the proximal and distal tubules under free-flow conditions after i.v. administration or micro-injection of vasopressin or aldosterone. Inulin clearence and the sodium: potassium urine ratio were measured at the same time. Special effects of vasopressin previously reported in young rats have been confirmed by the micropuncture technique and the site of its action apparently localized in different parts of the nephron.

VESTIBULAR AND EXTRAVESTIBULAR COMPONENTS OF THE CHAIN NEURO-HUMORAL MECHANISM OF VEGETATIVE RESPONSES TO GRAVITATIONAL EFFECTS. A.S.Dmitriyev. Inst. of Physiology, Byelorussian Academy of Sciences, Minsk, USSR.

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In the basis of vegetative reactions upon gravitational effects there lies a complex mechanism including vestibular (initiating) and extravestibular components consisting in its turn of reflex and humoral links. At rotation, changes in the function of internal organs, e.g. the mechanics of the intestine appear both under the influence of the afferent (vestibular) pulsation in the spinal cord, splanchnic and particularly diaphragmic nerves and due to the appearance of humoral (catecholamines) shifts which may affect on the effector and receptor of the internal organs and vessels, producing flows of visceral afferent impulses closing other visceral circular connections which are the beginning of new links in the chain neuro-humoral reaction. The role played by the cerebellum in effecting the labyrinth visceral components of intestine responses, and of the vessels and skin (cutaneous) - feather musculature accelerations is described.

INFLUENCE OF THE CHANGES IN BODY POSITION UPON LIMBS' AND ABDOMEN VASCULAR REACTIONS RECORDED BY RHEOGRAM AND PLETHYSMOGRAM. D.Dobrev and D.Stefanova. Higher Institute of Physical Culture, Sofia, Bulgaria.

Rheograms consequently recorded from right leg, left antebrachium and abdomen, as well as plethysmograms from right foot toes and left hand fingers are made in order to investigate the changes in the respective vascular area when altering body position. Data obtained show that vascular tonus of lower extremities increasesafter rising. Upright position being maintained a few minutes, a tendency of further increase of vascular tonus in capillary area is observed, especially. When a compressive bandage of lower extremities is applied, no orthostatic changes in their vascular tonus are observable. The changes in antebrachial vascular area after getting up or raising the hand are not so pronounced, even being sometimes opposite. Abdominal vascular changes are poor, too. An interpretation is given that vascular tonus changes in the different parts of the body, observed in the present investigation, are dependent on the extent of retention of blood in the different vascular areas as a result of the respective body position.

VENTILATORY RESPONSES TO CO₂ AND HYPOXIA AT DEPTH. <u>D. Doell and N.R. Anthonisen</u>, Respiratory Division, Royal Victoria Hospital, McGill University, Montreal, Canada.

Using a rebreathing technique, ventilatory responses to $\rm CO_2$ under both hyperoxic and hypoxic conditions were measured in four young men in a pressure chamber at one and four atmospheres absolute. The hyperoxic $\rm CO_2$ response curves were depressed in all subjects, particularly when surface values of ventilation exceeded 50 L/min. In two subjects the effect of depth was entirely due to decreased breathing frequency, in the other two both tidal volume and frequency were depressed at depth. $\rm CO_2$ responses during hypoxia (alveolar $\rm PO_2 = 40-50$ mm Hg) were also depressed. In three subjects the amount of ventilatory depression associated with depth was the same in hypoxia and hyperoxia, that is, when similar levels of ventilation were induced at the surface by $\rm CO_2$ alone and by the combination of $\rm CO_2$ and hypoxia, then at depth the same stimuli also produced similar levels of ventilation. Since depression of the hyperoxic $\rm CO_2$ response curve at depth was probably due to increased gas density and respiratory work, it is likely that the similar depression of the hypoxic $\rm CO_2$ response curve was also due to increased work of breathing. However, one subject demonstrated greater depression of the hypoxic $\rm CO_2$ response than the hyperoxic one; in this individual the hypoxic mechanism may either have been more sensitive to gas density or affected by inert gas narcosis. (Supported by the Canadian Defense Research Board and Medical Research Council of Canada).

426 STATISTICAL METHOD OF ANALYZING THE POWER SPECTRUM OF THE CORTICAL AND SUBCORTICAL EEG IN THE CAT. G. Dolce and H. Decker. Merck, Medical Research, Laboratory of applied neurophysiology, Darmstadt, FRG

A statistical method has been elaborated according to Smirnov and the iteration theory evaluating the power spectrum of the EEG derived from the cortex, limbic system and the mesencephalon in the immobilized cat by means of the fast Fourier transformation.

The electronic system of analysis described allows exact determination and qualification of spontaneous and evoked changes in the EEG of these formations.

CORRELATIVE STUDY OF MORPHOLOGICAL AND ELECTROCARDIOGRAPHIC CHANGES CARRELATIVE STUDI OF MORPHOLOGICAL AND EMBETROCARDICAL III CARRELATIVE STUDIO OF MARCHANDICAL III CARRELATIVE STUDIO OF MARCHANDICATIVE STUDIO OF MARCHANDICAL III CARRELATIVE STUDIO OF MARCHANDICATIVE STUDIO OF MARCHANDICATIVE STU

rol and vitamine Do in rats causes a severe myocardial dystrophy and vascular atheromatosis lesions in most animals. Electrocardiographic changes recorded prior to, during and after administration of the drugs were generally consistent with the morphologic changes but while their onset was already evidenced on the 3rd day of the experiment, the methods of investigation available failed to demonstrate at the same time the morphologic lesions. In rats having survived for 2 years after suppression of the carential diet, electrocardiographic disorders persisted in contrast with the apparently normal state of the animals.

CONTINUOUS RECORD OF A METABOLIC RESPONSE SYNCHRONOUS TO NEURAL ACTIVATION. M.Dolivo, B.Brauser and Th.Bücher. Inst.of Physiology, Univ.of Lausanne, Switzerland, and Inst.of physiological Chemistry, Univ.of Münich, Germany.

In correlating metabolism to function in nervous tissue, the usually recorded metabolic responses are delayed and slow as compared to the bioelectrical signs of activity and the spatial resolution is poor. To avoid these drawbacks we have applied to the isolated sympathetic ganglion of the rat the spectro-photometric methods developped for measuring the redox state of the pyridine nucleotides and cytochromes in the liver. The ganglion is mounted in a chamber between two quartz windows and continuously perfused. The neuronal activity can be driven by electrical stimulation and the electrophysiological response recorded. Surface fluorescence of the reduced pyridine nucleotides(PNH) is excited by a 366nm light beam and the emitted fluorescence measured. The changes of the redox state of the PNH have been correlated with well controled electrical and chemical stimulations. Thus a latency of less than one sec.is shown between onset of stimulation and metabolic response. The metabolic activity is proportional to the frequency of stimulation and to the number of activated neurons. A marked disagreement may occur between a well preserved action potential and an already deteriorating metabolic activity.

PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL BASIS OF THE SMOOTH MUSCLE CONTRACTION. J. Segarra Domenech. J. Santafe. A. Orts. J. Vila. J. Espluques. Dpt. of Pharmacology. Facultad de Medicina. Valencia. España.

The physiological and pathophysiological conduct of the smooth muscle must be identical theoretically with the management of the heart muscle. According to this conception we have studied: I-In the physiological activity the following have been evaluated: a-The contractility in relation to the rate of contraction, temp., and load; b-The Frank-Starling law.II-The pathophysiological activity has been studied producing a utilization(Propanolol) and supply (Dinitrophenol) insufficiency.100 muscles (uterus and ileus from Wistar rat) have been studied under isotonic activity. The evaluated parameters were interval-time, peak-time, Vmax., and Po., in Ia), and the extent of contraction in Ib) . The excitement was ACh.

When the load increases, Vmax. falls and Po rises. Increasing rate and temp. Vmax. rises and Po remains constant. The extent of contraction increases with the length. Propanolol (10,4.10 $^{-5}$ M) and Dinitrophenol (1,0.10 $^{-4}$ M) reduce the contractility shifting the F/V curve towards the left. The Ca. reverses the effect of Propanolol.

The perfomance of the smooth muscle under physiological and pathophysiological conditions is identical with the behaviour of cardiac muscle.

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HYPOTHALAMIC EVOKED POTENTIALS IN HEMORRHAGIC SHOCK. E. Dóra, I. Nyáry M. Kollai, A. G. B. Kovách Exper. Res. Dept. Semmelweis Med. Univ., Budapest, Hungary.

Function of the hypothalamus as well as other central nervous structures was studied in the state of hemorrhagic shock. The experiments were performed on dogs anaesthetized with chloralose. Potentials in the hypothalamic nucleus ventro-medialis were evoked by stimulation of nucleus amygdala, fornix and sciatic nerves. Arterial blood pressure, respiration, EEG and the hypothalamic evoked potentials were recorded. The hemorrhage was performed according to Wiggers. The amplitude of the evoked potentials decreased markedly in the first phase of hypotension. On continuing the bleeding the evoked potentials decreased in amplitude further and in some cases they disappeared entirely. In the period of retransfusion the evoked signals reappeared again but did not reach the original size.

THE SIGNIFICANCE OF Ca-INDUCED HIGH-ENERGY PHOSPHATE DEFICIENCY IN THE PRODUCTION OF NON-CORONAROGENIC MYOCARDIAL LESIONS. H.J.Döring, A.Fleckenstein O.Leder and E.Eschenbruch. Physiological Institute, University of Freiburg, Germany.

Cardiac structural integrity can only be maintained at the expense of phosphate bond energy. Accordingly structural damage occurs if the high-energy phosphate concentrations drop below a critical level due to insufficient ATP synthesis or to exhaustive ATP consumption. In rat hearts, following a single s.c. dose of 30 mg/kg isoproterenol, ATP is reduced to 1/2 and creatine phosphate (CP) to about 1/5 of normal for 2-3 hours and subsequently disseminated necroses develop. The fall in ATP and CP results from an isoproterenol-induced intracellular Ca overload which causes (a) excessive activation of Ca-dependent ATP-ases and (b) direct mitochondrial damage. Therefore the ATP and CP deficiency as well as cardiac lesions can be prevented if suitable doses of Ca-antagonistic substances (KCl, MgCl2, verapamil, D 600, prenylamine), which reduce the transmembrane Ca influx, are administered simultaneously with the isoproterenol. Conversely pretreatment with 9a-fluorocortisol, dihydrotachysterol or NaH2PO4, which sensitizes for cardiac lesions, potentiates the isoproterenol-induced Ca uptake and high-energy phosphate breakdown so that even an infarction-like pattern of necrosis may appear.

NATRIURETIC ACTIVITY IN HUMAN CEREBROSPINAL FLUID. Janice Dorn, Gary E. Kaufmann, Kemp Clark and John C. Porter. Depts. of Physiology and Surgery, Univ. of Texas (Southwestern) Medical School at Dallas, Dallas, Texas, U.S.A.

Although hyponatremia is a frequent concomitant of cerebral disease, its etiology is unknown. To investigate this phenomenon, fluid-electrolyte balance studies were per formed on a patient with post-traumatic meningitis who manifested hyponatremia (115-120 mEq/1), serum hypo-osmolality (235-241[mOsm]), and elevated levels of urinary sodium for 28 days. Cardiac, liver and renal functions, and excretion of 17-kestosteroids and 17-hydroxysteroids were within normal limits. The patient exhibited a normal response to sodium-poor diet, sodium-rich diet, fluid restriction and fluid overload. The sodium concentrations (121-123 mEq/1) and osmolalities (247 [mOsm]) of the cerebrospinal fluid (CSF) were slightly higher than serum levels, but lower than normal. Infusion of cerebrospinal fluid from the patient into the jugular vein of anesthetized rats increased the excretion rate of sodium, but did not change urine volume. Serum obtained from the patient, and cerebrospinal fluid from other patients did not alter sodium excretion in rats. The degree of natriuresis was directly related to the rate of CSF infusion. Infusion at .051 ml/min increased urinary sodium 4-fold, whereas infusion at .013 ml/min doubled sodium excretion. The natriuretic effect was observed in intact, hypophysectomized and adrenalectomized rats. The finding that CSF obtained from brain-injured patients with sustained hyponatremia is natriuretic in rats implicates a humoral substance of central neural origin in the development of the hyponatremic state.

BIOLOGICAL CHARACTERISTICS OF ERYTHROPOIETIN (ITS ANTIGENIC PROPERTIES AND PASSAGE THROUGH THE PLACENTA). M.Dorofteiu, A.Olteanu, V.Vasile, I. Baciu. Dept.of Physiology, Inst.of Pharm. and Med., Cluj, România.

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Erythropoietin given into Guinea pigs, generates precipitins and reagins. The purification degree of the hormone was investigated by immunelectrophoresis, using the antierythropoietin serum. The same immuneserum was utilized for testing the circulating erythropoietin by skin reactions assays. The hyperemic skin reactions of rabbits exposed to a decreased barometric pressure (simulated altitude of 5.500 m) was maximal after 4-6 hours.

The passage of erythropoietin through the placenta was investigated on pregnant bitches, with chronic isolation of somato-cephalic circulation, by causing a hypoxic ischemia of the head, in the last 5 days of pregnancy. Such animals presented raised level of blood erythropoietin. The new born dogs presented increased erythrocytes values and blood level of erythropoietin in comparison with control pups.

LEVEL AND PHYSICLOGICAL ROLE OF NUCLEIC ACIDS IN DOG SMALL INTESTINE MUSCULATURE. D.Dorogan (H.Aratei and Martoara Balan). Institute for Public Health and Medical Researches, Academy of Medical Sciences, Jassy, ROUMANIA.

Nucleic acids assayed with the Tanev and Markov spectrophotometric method, in the musculature of the duodenum, proximal portion of the jejunum and distal portion of the ileum in dogs. The results showed at least twofold increase in the content of DNA in the longitudinal musculature as compared to those in the circular musculature in all three intestinal segments studied. The DNA content showed a fairly wide scatter of the values (5-50 mg P % mg of moist tissue), unrelated to the musculature of any particular intestinal limb studied. The variable aspect of the level of nucleic acids was attributed to the functional role of remake of macromolecules, ferments and structural proteins used by functionning.

VASOCONSTRICTOR RESPONSES OF ISOLATED ANTERIOR TIBIAL ARTERY SEGMENTS. Philip Dow and D. L. Davis, Dept. of Physiology, Med. Col. of Georgia, Augusta, Ga. 30902, U.S.A.

Normally innervated in situ 1-2 cm segments of anterior tibial arteries of dogs were isolated from the remaining limb vasculature with inflow and outflow nylon catheters, and perfused with autologous blood at either constant inflow or constant pressure. Resistance changes, calculated from pressure-flow data, were used to assess segmental vasoconstrictor responses. Collateral circulation through vasa vasorum did not influence pressure-flow data. The sympathetic innervation of isolated segments was stimulated at the sciatic nerve level at 50-90 v and 2-3 msec pulse durations. Constrictor responses to 2-30 sec stimulation periods at frequencies of 1-100/sec were studied. Reproducible vascular responses were obtained at the lowest duration of stimulation periods, and over a wide range of stimulation frequencies. Short-term stimulation periods were used for assessing changes in vascular reactivity during infusions of levarterenol. Effects of resting intraluminal blood pressure levels on responses to short-term stimulation periods agreed with data obtained earlier when longer periods were employed (inverse relationships between resting intraluminal pressure and changes in resistance occurred), and indicated that the method of perfusion had little effect on the magnitude of resistance change in response to sympathetic stimulation over a wide range of resting intraluminal blood pressures. (Supported by grants from the Georgia Heart Assoc., and USPHS, Grant HE-00240).

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436 MOLECULAR MECHANISM OF FORCE GENERATION IN STRIATED MUSCLE. R. M. Dowben and L. C. Yu. Dept. of Biochemistry, Univ. of Bergen, Bergen, Norway; and Div. of Biomedical Sciences, Brown Univ., Providence, USA.

An electrostatic mechanism for force generation in striated muscle is envisioned which does not require bond formation between thick and thin filaments, nor movement of the cross bridges. The myosin heads, which project from the thick filaments and touch the thin filaments, possess a high negative surface charge density. Owing to their large dielectric increment, the thin filaments are polarized by the electric field generated by the myosin heads. The polarized thin filaments tend to move toward the center of the sarcomere. Myosin ATPase activity is increased in the overlap region to maintain the negative surface potential. Rapid proton migration probably is involved in producing the charge separation in the myosin heads. Thus, ATP hydrolysis provides the energy for muscle shortening. Calculations give estimated tensions in terms of the model that are comparable to those observed experimentally for vertebrate striated muscle.

THE INTERACTION OF NA AND H IONS WITH THE MEMBRANE OF THE RANVIER NODE. H. Drouin, I. Physiol. Inst. der Univ. des Saarlandes, 665 Homburg/Saar, Germany.

The current voltage relations of the sodium system of the Ranvier node of the frog are calculated according to a modified electrodiffusion equation derived by Agin (Biophys. J. 9:209 (1969). (1) The relations are determined by four parameters: (a) the potential difference at which the current is zero, (b) the limiting current at strong depolarisations, (c) the interaction energy of ions with sites in the absence of the trans-membrane electric field, (d) the electrodiffusion constant. (2) Reducing extracellular pH modifies two parameters significantly: (a) The limiting current at strong depolarisations is changed according to the dissociation curve of a weak acid. (b) The interaction energy as a function of pH can be described by the competitive exchange of Na and H ions with the membrane sites.

COMBINED BIOCHEMICAL AND ELECTROPHYSIOLOGICAL STUDIES OF THE S-POTENTIAL IN THE TELEOST RETINA. B.D. Drujan, G. Svaetichin and K. Negishi. Dept. Neurobiology. IVIC. Apartado 1827. Caracas, Venezuela.

Biochemical and electrophysiological studies of the S-potential behavior in the teleost retina showed its metabolic dependance (Q_{10} = 2-3). The potential could be blocked by agents which interfere with the oxydative metabolism of the retina like Azide, Cyanide and CO. The effect of the later could be reversed by light. The potential is strictly dependant on oxygen-presence. The respiration measurements of single horizontal cells with magnetic-diver techniques revealed that those cells which in fact showed to be the origin of the S-potential have an extremely low Q_2 -consumption rate as compared with other types of retinal cells. The electron microscopic studies of the horizontal cells show the presence of a few mitochondria only. Electrophysiological experiments reveal that the S-potential spreads laterally across an area which is in an anoxic state and remains unchanged up to 15 minutes in anoxia. The experimental results suggest that the oxygen-dependance of the S-potential is not due to the H-cell proper but rather takes place at the receptor level.

SECRETION OF MAGNESIUM BY THE DOG KIDNEY. Cristobal G. Duarte, Veterans Admin. Hosp., Nashville, Tenn. U.S.A.

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The fractional excretion of Mg was studied in dogs infused with either Ethacrynic Acid or Furosemide (5mg/kg prime and same/hr sustain)i.v. In other experiments Mg (1 gm MgSO₄ q.i.d.) was given i.m. for 7 days. Then Ethacrynic Acid or Furosemide in 20% mannitol was administered i.v. during Ca-Mg loading (40 mg/kg MgSO4 and CaCl2/3 hrs i.v.). The animals were volume expanded by i.v. Ringer's and urine was collected from the left ureter during 50% reduction in GFR by constriction of the left renal artery and after release of the constriction. Mean fractional excretion of Mg was 16% before and 55% during administration of Ethacrynic Acid or Furosemide, 64% after chronic Mg loading, 93% during and 133% after release of the constriction of the left renal artery constriction in Ca-Mg loading, Ethacrynic Acid-Furosemide experiments. This study demonstrates a secretory mechanism for magnesium evident during maximal diuresis, Ca-Mg loading and elevated filtered load of Mg. Secretion of Mg frequently occurred at high rates of Na excretion. Fractional excretion of Na closely paralleled Ca in these experiments.

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EFFECT OF FOREBRAIN LESIONS ON OVARIAN AND UTERINE HISTOLOGY AND CHOLIN-ESTRASE ACTIVITY OF MALE GENITAL ORGANS. S. Dua-Sharma, M.Savithramma, K.N. Sharma, and V. Gopal. Dept. of Physiology, St. John's Med. Col., Bangalore, India.

Rats with continuous estrus or preponderance of estrus produced by electrolytic lesions of medial septal and antero- and dorsomedial tha-lamic nuclei, had ovaries with no new follicles and a few corpora lutei in various stages of regression. Urine extracts of these animals pro-duced vaginal cornification in ovariectomised rats. Lesions of anteromedical amygdala and head of caudate nucleus led to continuous estrus, enlarged ovaries — full of corpora lutei with very few follicles, and distended uteri. Rats with preponderence of met and diestrus, after distended uterl. Hats with preponderence of met and diestrus, after lesions of nucleus accumbens, area offactorius, basolateral amygdala and lateral hypothalamus, showed larger ovaries containing varying number of corpora lutei and follicles, and smaller uteri than in nonlesioned controls. The cholinesterase (ChE) activity of testes and epidydimus of rats after bilateral surgical removal of offactory lobes, increased 4-6 days following lesions and then gradually diminished to a barely detectable level by 28-32 days. (Supported by Mysore SBMR Grant).

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Microelectrode study of hippocampal neuronal activity in awake rabbits (8-30 days) showed that the ability to habituation and dishabituation of reaction, which is a characteristic feature of hippocampal neurons in adult animals can be observed from the third week of life mainly in the CA3 field. In younger rabbits only the reaction to the first stimulus appeared in the form of a tonic inhibitory or excitatory modulation of spontaneous activity without directed dynamics in the course of repeated stimuli presentations. Simultaneously with the ability for signals discrimination manifested in the dishabituation of reactions, significant changes can be observed in CA1

ORIENTING REFLEX. N.V. <u>Dubrovinskaya</u>. Institute of Age Physiology, Acad. of Pedagogical Sciences, Moscow, USSR.

FUNCTIONAL MATURATION OF HIPPOCAMPAL NEURONS WITH SPECIAL REFERENCE TO

field. Phasic reactions to single stimuli first appeared in 13-15 days old animals greatly increase in number just to the 21-st day. These reactions reflecting the qualitative sign of the signal can be considered as a neuronal substrate of comparison of acting stimuli with the previous experience. Maturity of this substrate is one of the reasons of formation of hippocampal system of orienting reflex. This is displayed in the dynamics of CA3 neuronal reactions which began to correspond from the third week of life to the regularities of the orienting reaction. to the regularities of the orienting reaction.

442 REGULATORY MECHANISMS OF VISCERAL AFFERENTATION. P.Duda, J.Pavlásek. Inst. of Normal and Pathological Physiology, Bratislava, Czechoslovakia.

Splanchnic afferentation in the cat activates two spinal systems-propriospinal /PS/ and suprasegmental /SS/. This activity is reflected by early and late components of the viscerosomatic reflex in the thoracic region. Different speed of irradiation causes a fusion of both components in the lumbar region. Splanchnic activity converges on interneurones activated by somatic afferents as well. From the point of view of PS and SS systems following types of interneurones are discernable: a/activated by PS system b/by SS system c/by both of them. Splanchnic afferentation activates all these groups. PS and SS reflex mechanisms are activated by different subgroups of slowly conducting myelinated splanchnic afferents. It is possible to conclude that there is an intimate functional interconnection of PS and SS systems activated by somatic and visceral afferents.

443 EFFECTS OF VAGINAL STIMULATION AND LUTEINIZING HORMONE ON HYPOTHALAMIC SINGLE UNITS IN UNANESTHETIZED HYPOPHYSECTOMIZED RABBITS. DUFY, B., VINCENT, J. D., BENSCH, C., and FAURE, J. M. A. Lab. of Neurophysiology and Physiopathology, Sch. of Med., BORDEAUX 33, FRANCE.

In order to study the hypothesis that gonadotropin secretions of the adenohypophysis may exert short-loop feedback effects on the hypothalamus in the control of ovulatory mechanisms, we applied our techniques of chronic single unit recording to forty five conscious and freely moving female rabbits. In the rabbit ovulation can be induced by mechanical stimulation of the vagina. The variations in electrical activity of hypothalamic single neurones were studied during the first half an hour following vaginal stimulation, the period in which pituitary activation was presumed to occur. Since decrease in activity of ventromedial hypothalamic cells observed after vaginal stimulation in non hypophysectomized rabbits failed to occur when vaginal stimulation was performed in hypophysectomized rabbits, those unit firing changes could presumably be related to the release of the ovulatory hormone from the pituitary gland. When exogenous LH was administered intravenously to hypophysectomized rabbits, inhibitory responses were observed in ventromedial neurones. These responses appeared to be specific since they were independent of EEG changes.

THE EFFECTS OF POLYVINYL CHLORIDE (P.V.C.) TUBING ON ISOLATED PERFUSED LUNG PREPARATIONS. Helen N. Duke. Dept. of Physiol., Middlesex Hosp. Med. Sch., London, W.I.

Duke & Vane (1968) working with isolated cats lungs perfused with the animals own blood at constant volume inflow, showed that the normal hypoxic ventilatory pressor response did not occur if the perfusion circuit was partly made of new P.V.C. tubing. The tubing used was listed as surgically non-toxic. After the tubing had been boiled in chromic acid and thoroughly washed, no adverse effects were demonstrated. The experiments now reported show that additions of aliquots of plasticiser (acetyl - tri - n - butyl citrate) or tubing, incubated at 38°C for two hours in plasma or saline abolished the hypoxic pressor response. Control experiments with plasma or saline were without effect, as were additions of the stabilizer or lubricant. These results show that this plasticiser inhibits the pulmonary hypoxic pressor response, a factor which must be taken into account in procedures such as cardiac bypass and renal dialysis in man. The results of further experiments with different types of tubing will be described.

Duke, H.N. & J.R. Vane (1968). Lancet. 21-23.

VARIATIONS IN FIBRINOLYTIC ACTIVITY AND BLOOD PLATELETS FOLLOWING EXERCISE IN HIGH PERFORMANCE SPORTSMEN. <u>Elena Dumitrescu-Papahagi</u>, <u>Zoia Demetrescu</u> (with technical assistance of Gabriela Hosu). "D. Danielopolu" Inst. of Physiology, Academy of Medical Sciences, Bucharest, Romania.

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Variations in fibrinolysis, blood platelets, red cell count, hematocrit as well as in MCV, MCH and MCHbC were measured in blood specimens sampled from high performance rowers (lo males and lo females, aged 19 to 24 years) prior to and lo min after stationary rowing on a basin during 45 min. A slight elevation in hemoglobin and hematocrit was noted in both groups as well as an increase in the leukocyte count in males versus a slight decrease in females. Significant changes were found in platelet counts and in fibrinolysis in both groups: following exercise, a constant finding was a twofold rise in blood platelets with a simulatenous marked acceleration of fibrinolysis. This acceleration was taken as a tendancy of the body to restore homeostatic balance, deeply altered by an increase in number and adhesive force of the platelets. It is believed that elevation of body temperature induced by exercise could possibly stimulate the hypothalamic higher organo-vegetative centers which activate blood plasmin precursor production .

EFFECT OF HIPPOCAMPAL STIMULATION ON THE PLASMA TSH AND CORTICOSTERONE RESPONSES TO ACUTE EXPOSURE TO COLD IN THE RAT. A. Dupont, E. Bastarache, E. Endröczi and C. Fortier. Endocrine Lab., Dept. of Physiology, Fac. of Med., Laval Univ., Quebec, Canada.

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As opposed to other environmental stimuli which simultaneously enhance ACTH release and depress TSH secretion, exposure to cold concurrently stimulates the two tropic hormones (Fortier et al., Can. Med. Ass. J., 103, 864-874, 1970). Seven days after the stereotaxic implantation of bipolar epoxylite-insulated stainless steel electrodes in adult male rats, stimulation of the dorsal hippocampus, with a current of $1.3 - 1.5 \, v$, $10 \, cps$ and $0.1 \, msec$ pulse duration, was found to inhibit the secretion of ACTH (as indicated by the plasma corticosterone concentration) and to enhance the secretion of TSH (as shown by the plasma TSH level) associated with a 20 min exposure to cold (-5° C). These findings suggest that the concurrent stimulation of ACTH release and inhibition of TSH secretion induced by nonspecific stress (which tends to oppose the specific "sensory" component of exposure to cold) are possibly related to depressed hippocampal activity and emphasize the necessity of reassessing the role of the hippocampus and of other structures of the limbic system in the control of ACTH and TSH secretion. (Supported by Canadian MRC grant MT-1205).

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SLOPE AND INTERCEPT OF THE LINEAR RELATIONSHIP BETWEEN CARDIAC OUTPUT (Q) AND OXYGEN CONSUMPTION (\dot{v}_{02}) . J. Durand, J. Mensch, J.P. Bourdarias. Med. Sch. Paris, FRANCE.

The linear relationship between \dot{Q} and \dot{V}_{02} during study state of submaximal exercise can be written: (1) $\dot{Q}=k\dot{V}_{02}+\dot{Q}_{0}$ (k slope, \dot{Q}_{0} intercept). On the other hand, the equation describing the Fick principle can be rearranged as: (2) $\dot{Q}=\dot{V}_{02}/Ca_{02}+QC\bar{v}_{02}/Ca_{02}$, $(Ca_{02},C\bar{v}_{02})$; 02 content in arterial and mixed venous blood respectively). Comparing (1) and (2), $QC\bar{v}_{02}/Ca_{02}$ approximately. pears to be either a constant or a linear function of v_{02} . To determine which of these mathematical solution was experimentally verified, and hence to give a physiological meaning to k and \hat{Q}_0 in (1), a large number of observations were collected. The conclusions are : (i) $QC\bar{v}_{Q_2}/Ca_{Q_2}$ is constant whatever \hat{v}_{Q_2} i.e. the Q_2 flow returning to the lung from the tissues, expressed in term of arterial blood flow, is independant of the total metabolic activity and represents the origin \hat{Q}_0 of (1). (ii) The slope k is equivalent to $1/Q_0$. valent to $1/CaO_2$. This agrees with the experimental findings showing alterations of slope and/or intercepts with posture, sex, age, and abnormal environmental conditions such as altitude and heat.

FUNCTIONAL ORGANISATION AND TRANSMISSION MECHANISM IN THE THALAMIC VP 448 NUCLEUS. R.A. Durinian. Inst. of Physiology, Medical Academy of Sciences, Moscow, USSR.

There is there functional types of cells in the VP: relay cells (R) and two interneurons. The antidromic responses by stimulation of the SI-S2 cortex have only the short latency (no more 6 msec) lemniscal units (R). The units with long latency (6-12 msec) by the same cortical stimulation have shown orthodromic responses and may be called second type units (S). Among S-cells there are some units with wide receptive fields; some of them were activated through the spino-thalamic system. Besides the local system for direct transmission to the cortex (R) there is in VP the intrinsic system of units (S) with wide afferent convergence. Such pattern could provide in VP the both mechanisms of sensory disctimination pattern could provide in vr the both mechanisms of sensory disctimination and integration. R-cells are the relay units not only for cortical transmission but also for intrinsic system of VP units. The transmission mechanism of VP exept (R) and inhibitory (I) interneurons (Andersen et all) has one more interneuron-excitatory. This cells are rhythmical active (8-12 p.sec) units (RA) and their activity interrupted at the period of evoked discharges R-and I-cells. The transmission mechanism with two interneurons will be discussed.

FAT-FREE MASS, GROSS BODY WEIGHT AND ADDED LOADS, RELATIVE TO METABOLIC RATE IN 449 STANDARDIZED EXERCISES. By J.V.G.A. Durnin and J. Womersley. Institute of Physiology, The University, Glasgow, W.2, Scotland.

Although accounts of the oxygen consumption during walking at different speeds and during load carriage form part of the classical literature in physiology (Atzler & Herbst, 1927; Benedict & Murchhauser, 1915; Douglas & Haldane, 19k2; Margaria, 1938), previous studies have not made it possible to assess the results in relation to body composition and in particular to the quantity of adipose tissue. In the present study the subjects were 22 young men and 23 young women whose body fat content was measured by densitometry. Their oxygen consumption was assessed (1) while they walked on a they density in their oxygen community was assessed (1) while they wanted our and (2) while they carried loads of 0, 10,15 and 20 kg at $2\frac{1}{2}$, 3,4 and $4\frac{1}{2}$ m.p.h. Results have been calculated as ml 0, per kg of gross body weight and per kg of fat free mass. Oxygen uptake was found to be directly related to total weight carried, that is, body weight plus any load. The fat component of the gross body weight was equivalent to an inert load in this respect. There was no difference between the sexes.

OBSERVATIONS ON C .RO-INTESTINAL METABOLISM. A.O. Durotoye and J. Grayson, Department of Physiology, Unive sity of Toronto, Canada.

In a series of 20 dogs (nembutal anaesthesia), aortic, portal venous and duodenal temperatures were measured; also portal blood flow (electromagnetic flowmeter) and arterioportal venous 02 and glucose differences. Mean resting heat production (flow X aorticportal temperature difference) was 63.9 cals/min. Mean 02 uptake was 11.0 ml/min. Mean glucose uptake was 20.0 mgm/min. On basis of glucose metabolism, 02 uptake could account for 48.2 cal/min, significantly lower than actuality. On basis of oxidation glucose uptake gave a figure of 77 cals/min, significantly higher than actuality. Injections of glucagon (5 ug/kg, i.v.) markedly increased aortic-portal glucose differential and gastro-intestinal glucose uptake. There was no effect on 02 uptake or heat production. Injections of glucose (0.5 gr/kg) which raised blood glucose to approximately same levels as glucagon, increased portal glucose to levels usually higher than aortic suggesting an inhibition or even reversal of the glucose uptake process. There was no effect on O2 consumption or heat production. The mechanisms of heat production in the g.i. tract remained not fully explained. The effects of glucose may be due to endogenous insulin secretion. A metabolic function in terms of hormonally controlled glucose uptake, storage and release is postulated.

INHIBITION OF THE HISTAMINE INDUCED GASTRIC ACID OUTPUT BY HEPARIN IN VERVET MONKEY. Brahma Dutt. Physiol. Dept., Makerere Univ. Med. Sch., Kampala, Uganda.

Histamine and heparin interact in many biological phenomena. Heparin suppression of gastric acid response to histamine has been shown in man, dog and guinea-pig. Heparin given to facilitate blood pressure recording in vervet monkeys affected the gastric acid Output stimulated by histamine. To study this inhibition in chloralose anaesthetized vervet monkeys (14) gastric acid output was estimated in response to continuous intravenous infusion of histamine base in 12.5 to 400 ng/Kg/min doses, or histamine with heparin 2 to 4 international units/Kg/min. These denervated acute preparations had their pylorus ligated stomachs siphoned via oesophagostomy in the neck. Results showed no statistically significant (p:0.25) increase in resting gastric acid secretion upon infusion of heparin alone. While 25 ng of histamine alone elicited a p:0.005 significant acid response, 100 ng histamine given with heparin produced a p:0.001 acid output. Heparin induced 79%,74%,84% and 70% reduction in acid yield at 50, 100,200 and 400 ng histamine with p values of .005, <.001, .001, <.001 respectively. In the non-heparinised and the heparinised animals 40 and 29 observations were to get the correlation coefficients of 0.8342 and 0.7583 respectively between acid output and histamine doses (p:<001 for both). Extrapolation of the regression lines from the above date suggested that the mechanism of this heparin induced inhibition of gastric acid was a combination of heparin and histamine rather than blocking of parietal cells. Protamine sulphate, a heparin antagonist, blocked or even reversed the observed inhibition. Heparin did not affect the histalog induced acid production.

CENTRAL EFFECTS OF OUABAIN IN CATS. S.N. Dutta, B.N. Basuray and S.N. Pradhan, Howard Univ. Col. of Med., Washington, D. C. 20001, U.S.A.

Current evidences suggest that cardiotoxic and respiratory effects of i.v. infusion of ouabain are related to its excitant action on the central autonomic mechanisms. In the present study the central effects of ouabain were investigated in c-chloralose anesthetized cats after its administration through a cannula-electrode implanted stereotaxically into either the lateral cerebral ventricles or ventromedial hypothalamic nucleus (VMH) or dorsal nucleus of vagus (DNV). Injections into the VMH or the DNV were made only when their electrical stimulation evoked either a pressor or a depressor response. Femoral arterial pressure, electrocardiogram (Lead II) and respiration were recorded. In majority of cats, microinjections of ouabain (16-40 Aug/kg) into the VMH or the INV produced cardiac arrhythmias and respiratory depression leading to death. Lethal doses of ouabain in these animals were significantly smaller than those following intraventricular and i.v. injections. These data indicate that central autonomic sites are involved in the cardiac arrhythmias produced by ouabain.

PLASMA OXYTOCIN CONCENTRATION AND FIRING RATES OF IDENTIFIED PARAVENTRICULAR NEURONES IN RAT DIENCEPHALIC ISLANDS. R.E.J. Dyball and R.G. Dyer. Dept. of Anatomy, University of Bristol, England.

Estimates of the concentration of oxytocin in the plasma of oestrous female rats under urethane anaesthesia varied between 126 and 394 µu/ml with 95% confidence limits between 94 and 458 µu/ml. In contrast, plasma from diencephalic island preparations (Cross & Kitay, Expl. Neurol. 19: 316, 1967) made from a group of similar animals contained no detectable milk-ejection activity and the sensitivity of the assay preparations made it possible to give a figure of <47 µu/ml for the plasma concentration of oxytocin under these conditions. In addition electrical recordings were made from antidromically identified (Dyball, J. Physiol., Lond. 203: 3P, 1969) paraventricular neurones in intact animals and in diencephalic islands. Nineteen of the twenty-six units in island preparations were quiescent compared with three out of twenty-five in the controls. Thus, in contrast to its effect on the majority of hypothalamic cells, deafferentation caused a significant (P<0.001) reduction in the spontaneous activity of paraventricular neurones. Since we found no significant difference in neurohypophysial oxytocin content between island preparations and intact animals, these observations are consistent with the hypothesis that an increased action potential frequency in paraventricular neurones is associated with oxytocin release.

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ON EMOTIONAL CONDITIONED REACTIONS. N.Dzidzishvili. Inst. of Physiology, Georgian Academy of Sciences, Tbilisi, USSR.

The conditioned emotional reactions are easily formed on the basis of limbic structure stimulation in cats. Similar reactions are worked out in rabbits when only some limbic formations are stimulated. However, the reactions of the rabbits differ from those of the cats: they disappear very easily and are not reversed even after numerous combinations of conditioned and unconditioned (limbic) stimuli. When dorsal or ventral hippocampus, pyriform lobe or ventromedial hypothalamus are stimulated in rabbits, emotional conditioned reaction cannot be formed for these stimuli never evoke any typical emotional behaviour. It is assumed that absence of such a behaviour is due to insufficient phylogenetic development of neocortex in rabbits. The assumption is confirmed by experiments made on cats with removed neocortical associative areas: their response to the limbic stimulation does not bear the characteristic features of motivational (emotional) behaviour. On the basis of stimulating e.g. the dorsal hippocampus in these cats there is no longer possible to form conditioned fear reaction as it was the case with the intact rabbits.

455 MITIGATION OF ETHANOL-INDUCED FATTY LIVER BY INCREASED CALORIGENESIS. Charles J. Eagan, Hugh T. Bainter, and Don L. Netzinger. Colo. State Univ., Fort Collins, Colo. 80521 USA.

It was not known whether the lipolytic effect of increased caloric expenditure would apply to hepatic steatosis caused by ethanol consumption. In this study, ethanol-induced hepatic lipogenesis was compared between sedentary rats at room temperature and other groups, either exercised or cold exposed. Two liquid diets were used: "dextrin", comparable to the North American diet in proportion of calories from fat (35%), protein (18%), and carbohydrate (dextrin) (47%); "alcohol", of identical composition except that ethanol replaced dextrin isocalorically to the extent of 36% of total calories. An Alcohol-Sedentary group (AS) was fed the alcohol diet ad libitum and a Dextrin-Pair-fed group (DP) the dextrin diet isocalorically on a weight-specific basis. After 3 weeks on the alcohol diet, liver lipid content for AS, 9.87%, was almost twice that for DP, 5.43%, (P<0.01). Alcohol-Exercise (AE) and Alcohol-Cold (AC) groups consumed the same amount of ethanol as AS; AE was run on a treadmill for 4 hr/day at 1.6 km/hr; AC was exposed to 10°C for 20 hr/day; extra calories required by both groups were supplied from dextrin diet. Liver lipid content for AE, 7.45%, was greater than that for DP (P <0.01) but less than that for AS (P <0.01); the value for AC, 5.66%, was similar to that for DP and, hence, significantly less than that for AS (P <0.01). It is concluded that increased caloric expenditure inhibits the development of alcoholic fatty liver. (Supported in part by Faculty Research Grant No. 858, Colorado State University, 1969)

PHYSIOLOGICAL SIGNIFICANCE OF THE CUTANEOUS MECHANORECEPTOR INPUT TO THE CEREBELLUM. J.C. Eccles, N.H. Sabah, R.F. Schmidt and H. Taborikova. Depts. of Physiology and Biophysics, State University of New York at Buffalo, New York 14226.

Selective and adequate stimulation of mechanoreceptors in the cat's hind limb, both of rapidly and slowly adapting receptors of the foot pads (RAR and SAR) and of the hair follicle receptors (HFR) evoke mossy fibre (MF) and climbing fibre (CF) responses of cerebellar Purkyne cells. In lightly anaesthetized and unanaesthetized decerebrate cats the characteristics of the unitary spikes of Purkyne cells were studied by time histograms and their cumulative distributions. The CF pathway transmits the activity of RAR and HFR. For any particular Purkyne cell the receptive fields of these phasic receptors are contiguous and sharply demarcated. A depression follows CF-evoked responses and during prolonged repetitive stimulation (vibration) only the initial afferent volley is transmitted by CFs. transmit to Purkyne cells via MF and not CF pathways. Pressure pulses of several seconds duration give prolonged SAR discharges which by mediation of MF pathways either enhance or depress the spontaneous action of Purkyne cells for the duration of the pressure. Other components of the MF pathway transmit activity from the RAR and the HFR. Recordings from single MFs showed that part of this input follows high frequency stimulation (vibration) of phasic receptors, whereas other MF give responses similar to those from CF. This precise selective information from cutaneous receptors evidently is required for the cerebellar performance in fine control of posture and movement. CF input being phasic is related to movement, whereas MF input would have a dual function.

MEMBRANE RESISTANCE AND ELECTRICAL EXCITABILITY IN PARAMECIUM. R. Eckert, Y. Naitoh and K. Friedman. Department of Zoology, University of California, Los Angeles 90024, USA.

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Excitability of the cell membrane of \underline{P} . $\underline{caudatum}$ was investigated with intracellular methods in dilute solutions of $CaCl_2 + KCl + lmM$ tris buffer, pil 7.2. Depolarization produces a graded regenerative response which results from a transient inward calcium current (Eckert and Naitoh, 1969, 3rd Int. Biophys, Congr., Cambridge, p. 257). The ratio $[K]_o/[Ca]_o^2$ was adjusted to 1,2,4,8 or 16 in each of two series, one at constant $[Ca]_o$ (=lmM), the other at constant $[K]_o$ (=2mM). In both series the input resistance increased as the ratio decreased, and was independent of the absolute $[Ca]_o$. Increased input resistance was correlated with an increase in the amplitude (resting potential to peak) and rate of rise of the maximally excited response. Ba++ increased the input resistance in concentrations of lmM or less. This was accompanied by conversion of graded excitability to an all-or-none, barium-sensitive action potential. Injected tetraethylammonium neither increased the input resistance nor converted the response to all-or-none. In conclusion, $[Ca]_o$ relative to $[K]_o$ determines the input resistance of $\underline{Paramectum}$ and hence the degree to which the regenerative inward current is short-circuited by outward current.

Measurement of Corneal Oxygen Consumption after Freeze Preservation of Corneal Tissue to -196°C. Henry F. Edelhauser and Diane L. Van Horn. Medical College of Wisconsin, Milwaukee, Wisconsin 53233

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A study has been made to determine corneal oxygen consumption (Q02) of fresh and cryopreserved rabbit corneas. Corneas were cryopreserved according to the method of Kaufman and Capella (J. Cryosurg., 1:125, 1968). These authors have successfully utilized human corneas preserved by this method for transplantation. The method consists of incubating the cornea for 10 min at $4^{\circ}\mathrm{C}$ in each of a series of four hyperosmotic cryoprotective solutions with increasing concentrations of DMSO and sucrose made up in 25% human serum albumin; frozen in a controlled-rate freezer to -79°C, stored at -196°C in liquid nitrogen and, when needed, carefully thawed in a water bath at 60°C for 50 seconds and incubated in 25% albumin for 10 minutes. Q02 measurements of fresh and frozen corneal tissue were made with a modified biological oxygen monitor (YSI Model 53) utilizing a Clark O2 electrode. The Q02 of fresh corneal tissue is 0.799 $^{\pm}$ 0.03 ul 02/mg dry wt and the cryopreserved tissue 0.369 $^{\pm}$ 0.6 ul 02/mg dry wt. When the epithelium of the cornea is removed prior to Q02 measurement and cryopreservation, the Q02 of the fresh cornea w/o epithelium is 0.387 $^{\pm}$ 0.03 ul 02/mg dry wt as compared with the frozen tissue of 0.117 $^{\pm}$ 0.03 ul 02/mg dry wt. The results show that freeze preservation of the corneal tissue does decrease the Q02 by 50%. These Q02 measurements will be correlated with ultrastructural appearance of the corneal epithelium, stroma and endothelium following the cryopreservation procedure. (Supported in part by USPHS, NIH grant EY-00428)

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POTASSIUM TRANSPORT BY RAT COLON. C.J. Edmonds and Diana E.M. Pilcher. MRC Dept. of Clinical Research, Univ. Col. Hosp. Med. Sch., University Street, London, England.

Colonic epithelium possesses active and passive mechanisms for potassium transport which are under hormonal control. The present investigation was undertaken to determine more about these processes by a study of potassium kinetics in intestinal epithelium of the rat. An in vivo technique was developed which combined pulse labelling of epithelial cells, either from the luminal side or from the serosal side by intraarterial injection of K.42, with the use of miniature GM counter to measure the radio-isotope turnover rates. The results showed that components with fast and slow turnover rates were present. Analysis of the results indicates that (i) the slow component probably represents the main mass of potassium of the epithelial cells. Potassium enters this mass easily from the serosal side but the mucosal side is relatively impermeable. The potassium actively secreted into the lumen by the colonic mucosa comes largely from this component. (ii) Much of the potassium crossing the epithelium appears to pass through 'shunt' pathways without mixing with the main mass of potassium in the epithelial cells.

460 UPTAKE OF SOME PUTATIVE NEUROTRANSMITTERS INTO RABBIT RETINAL STRUCTURES. B. Ehinger. Departments of Experimental ophthalmology and Histology, University of Lund, Sweden.

The rabbit retina was exposed in vivo or in vitro to tritiated GABA, glycine, aspartic acid, glutamic acid, 1-dopa, dopamine, and histamine. The tissue was freeze-dried, fixed in dry gaseous formaldehyde, embedded in plastic, sectioned, and covered with autoradiographic stripping film. Diffusion or extraction artefacts were shown to be negligible with the procedure. After exposure to glycine radioactivity appeared in cells with position and spread like the amacrines. A similar, although not altogether identical, group of cells became radioactive after exposure to GABA. In both cases some ganglion cells became radioactive. With glutamic or aspartic acid only Müller (glial) cells became radioactive. I-dopa and dopamine caused radioactivity in cells with the position and spread of the retinal adrenergic neurons. Histamine did not give any localized radioactivity except in the retinal pigment cells. Taken together with physiological and pharmacological results, it can be suggested that some amacrine cells operate with GABA as neurotransmitter. Possibly glycine is also the neurotransmitter of a different set of amacrines.

DIFFERENCE BETWEEN ADAPTATION OF CORONARY FLOW TO TREADMILL EXERCISE AND TO EATING.
W. Ehrlich, J. Tosheff, J. V. Brady. Johns Hopkins Univ. Sch. of Med., and Sch. of Hyg.
and Publ. Hith., Baltimore, Maryland, USA.

The adaptation of flow in circumflex branch of left coronary artery (CF) and of other circulatory functions to exercise was studied in a total of 34 trials with 3 dogs. The dynamic pattern of changes in CF and other circulatory functions evaluated in successive two-second intervals and documented in mean values from all exercises with each animal are compared with the pattern of adaptation to eating elucidated in 44 trials with the 3 dogs. The onset of exercise and of eating as well as each other period of heart rate increase is accompanied by a biphasic CF change: a significant decrease of CF followed by a significant steep increase of CF. In adaptation to exercise, the short decrease of CF is followed by a prolonged increase forming essentially the baseline for any further CF change during exercise. The comparison of all circulatory changes leads to the conclusion that the CF flow changes during exercise are caused substantially by changes of coronary resistance (CR) which, after an initial rise, stays lower during the exercise period studied. In adaptation to eating, however, the short decrease of CF is followed by a transient increase. Subsequently, the CF returns to values only slightly higher than the rest values. The CR shows a short biphasic reaction and then stabilizes for the rest of the eating time to values higher than the rest values. As much as the eating activity after the first 8 seconds is accompanied by a slightly enhanced CF, this is caused by the simultaneous blood (Supported by NIH Grant #HE 06945-09) pressure rise.

462 RENIN RELEASE AND AUTORECULATION OF RENAL BLOOD FLOW. I. Eide, E.W. Løyning, and F. Kiil. Inst. Exper. Med. Res., Univ. of Oslo, Ullevaal Hosp., Oslo, Norway.

Renin release was measured in anesthetized dogs during stepwise mechanical reduction of renal perfusion pressure. Within the range of autoregulation of renal blood flow (RBF), renin release increased on average from 2.9 to 14.6 µg/min. RBF decreased with further stepwise reductions of arterial perfusion pressure, but renin release remained constant. Raising ureteral pressure to 42-65 mm Hg increased RBF on average by 27% and renin release from 3.5 to 9.1 µg/min. High ureteral pressure, whether or not combined with constriction of the renal artery, did not increase renin release more than arterial constriction alone.

It is concluded that release of renin is related to the dilatation of afferent arterioles. Such dilatation becomes maximal both during arterial constriction and ureteral obstruction before RBF is reduced.

INDUCTION OF DELAYED IMPLANTATION IN RATS WITH HALOPERIDOL, TRIPERIDOL AND FLUPHENAZIN-ENANTAT. N. Einer-Jensen. Inst. of Physiology, Odense University, Odense, Denmark.

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3-12 mg/kg Haloperidol dosed daily to pregnant rats from day 0 (the day when sperms were observed in vaginal smears) induces delayed implantation measured as prolonged pregnancy or, if the pregnant rats are sacrificed on day 20, as diminished weight of the foetuses. Our experiments showed that the Haloperidol administration interferes with the induction of the implantation (days 0 and 1) but not with the developing implantatory processes (day 4 or later). Diminished weight of the foetuses can also be obtained with 18 mg/kg Triperidol dosed 0-3 or with a single injection on day 0 with 12.5-50 mg/kg Fluphenazin-enantat.

EFFECTS OF BLOCKING THE AUTONOMIC NERVOUS SYSTEM DURING EXERCISE. B.Ekblom, A.N.Goldbarg and P .- O. Astrand. Dept. Physiol. Gymnastik- och idrottshögskolan, Stockholm, Sweden.

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The influence of the autonomic nervous system on the oxygen transport system during exercise was investigated in 14 subjects by means of bicycle work (submaximal and maximal loads) during: 1) control (C), 2) after parasympathetic blockade (PSB) with atropin (2.5 mg iv), 3) after beta-adrenergic blockade (BAB) with propranolol (Inderal^R, 10 mg iv) and 4) after double blockade (DB) with both drugs.

Maximal VO2 decreased 6% (p < .05) after DB and the time during the maximal work was

decreased. In contrast, single blockade did not affect maximal VO2, but the time during maximal work was reduced after BAB. At rest and during submaximal work VO2 was not affec-

ted by any treatment.

At rest PSB increased heart rate by 40 beats per minute (60%), but this effect became less pronounced as load increased and maximal heart rate was unchanged.BAB caused a significant decrease in heart rate at rest, which became more pronounced as load increased. After DB heart rate at rest increased, was similar to C at 25% of maximal \dot{v}_{02} and thereafter progressively decreased compared with C up to maximal work.

Both branches of the autonomic nervous system seem to exert similar roles in the setting of the heart rate during exercise at a load of about 40% of maximal $\dot{\text{VO}}_2$.

OXYGENATION OF ISOLATED GASTRIC PREPARATIONS. M. Ekelund and K.J. Öbrink. Inst. of Physiology and Med. Biophysics, Biomedical Center, Univ. of Uppsala, Sweden.

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Isolated gastric mucosae of mammals in Ringer's solutions bubbled with oxygen at atmospheric pressure show signs of hypoxia, whereas those of frogs seem to function in a normal way. Production of lactic acid and active transport of sodium are seen in the hypoxic states. To study the oxygen transport from the surface of the preparation to the cells in the mucosa the rate of movement of oxygen from the serosal to the mucosal side of the preparation was studied in a two-chamber system at constant temperature. On the serosal side oxygen was supplied at atmospheric pressure and on the mucosal side the oxygen tension was continuously monitored. To avoid a transport into the cells the oxygen consumption was cut out by cyanide. The extracellular oxygen transport was found to be much greater in the gastric mucosa of frogs than in the isolated stamped of mice. This may indicate the reason for the difficulty of walks. isolated stomach of mice. This may indicate the reason for the difficulty of using isolated gastric preparations of mammals.

466 SODIUM EXCRETION DURING ORAL WATER LOADING IN THE TROPICS OYINADE ELEBUTE (NIGERIA) DEPT. OF PAEDIATRICS COLLEGE OF MEDICINE LAGOS

Sodium excretion is usually increased in defence of extracellular fluid expansion. Natriuresis was absent in 20 normotensive male Nigerians during oral water loading of 20 ml/kg on a standard (150 - 200 meq) hospital diet when excretion was controlled for posture, time of day and physical activity. Chloride excretion fell from prediuresis period whilst potassium excretion was unchanged. Urine flow rate and free water clearance increased progressively to a maximum. Exaggerated water diuresis and diminished sodium excretion is peculiar to inhabitants of hot tropical climate.

467 CONTRACTILE FUNCTION AND STRUCTURE OF GUINEA-PIG TAENIA COLI AFTER EXPOSURE TO -79°C IN UNFROZEN MEDIA. B.C. Elford and C.A. Walter. Clin.Res.Ctr. Lab., and Natl. Inst. Med.Res. London, NW7. England.

Isolated strips of smooth muscle were incubated in solutions of increasing concentrations (up to 60% w/v) of dimethyl sulphoxide (DMSO), and gradually cooled to -79°C for 15-20 hrs. With respect to the concentrations of sodium, potassium and chloride, the ionic composition of the bathing media was similar either to that of Krebs solution or to the intracellular fluid. Use of the potassium-rich media which were buffered with glycerophosphate, TES or PIPES (N-tris-(hydroxymethyl)-methyl-2-amino- or piperazine-NN'-bis-2-ethanesulphonic acids) gave marked improvement both in the isometric contractile response of the muscles to histamine on rewarming to 37°C, and in the morphology of the cells as shown by electron microscopy. In addition to the varying concentrations of DMSO, these solutions contained: 1)calcium, magnesium, bicarbonate, phosphate and glucose at the same molar concentration as in normal Krebs solution, 2)sodium 8. 4mM, potassium 165.5mM, chloride 56.9mM and 3)either glycerophosphate 53.9mM, TES 196.3mM or PIPES 59.5mM. The contractility of muscles cooled and rewarmed in the high-K PIPES media was comparable with that of fresh muscle, and the appearance of the cells, of which only a few were disorganised, was similar to that of cells fixed immediately after dissection. By contrast, there was obvious aggregation of the myofibrils in cells cooled in the Krebs-based media, and, although pinocytotic vesicles could still be seen, the cell membranes appeared to be broken.

REGULATION OF SWEAT GLAND FUNCTION AFTER SHORT TERM HEAT ACCLIMATION. R.S. Elizondo*, & R.W. Bullard. Dept. of Anatomy & Physiology, Indiana Univ. Bloomington, Indiana, USA. The purpose of this investigation was to obtain information as to whether the changes in sweat gland function associated with short term acclimation are due primarily to changes in the sensitivity of the central nervous system regulatory center or to changes in the sensitivity of the peripheral detecting units which provide information to the central nervous system. The technique of resistance hygrometry was used to study the dynamics of sweat gland function following short term heat acclimation. Two functional tests were performed before and after short term acclimation. One of these functional tests consisted of 7% CO2 inhalation for 4 minutes which was used as a central stimulus for sweating. The second functional test consisted of a study of the reflex responses of the sweat glands to regional cooling of the skin. Seven percent CO2 inhalation for 4 minutes tended to be a more effective central stimulus for sweating after short term acclimation. The sweating rate increase upon $\rm CO_2$ inhalation averaged 60% of the initial sweating rate and after short term acclimation it was 90%. Therefore, the identical stimulus caused a greater change in sweat production following acclimation. In the reflex test the lower leg placed in a water bath was isolated by arterial occlusion to establish the neural nature of the response. Depression in generalized reflex sweating dut to cooling of the lower leg was 20% less after acclimation suggesting a slight decrease in the sensitivity of the peripheral thermal receptors following short term heat acclimation.

LACK OF EXCLUSIVELY FUSIMOTOR & AXONS IN FLEXOR AND EXTENSOR LEG MUSCLES IN THE CAT. P. H. Ellaway, F. Emonet-Dénand, M. Joffroy and Y. Laporte. Laboratoire de Physiologie, Faculté de Médecine, Toulouse, France.

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Stimulation of single motor axons supplying tibialis anterior, extensor longus digitorum and flexor hallucis longus muscles with a conduction velocity superior to 50 m/sec may elicit discharges in spindle afferent fibres. This action could be ascribed to : (1) contraction of some extrafusal muscle fibres deforming spindle sensory endings ; (2) contraction of intrafusal muscle fibres innervated by motor axons supplying both extra- and intrafusal muscle fibres (β innervation) ; (3) contraction of intrafusal muscle fibres exclusively innervated by these fast conducting axons.

This last possibility can be excluded because it was found that, out of a total of 1813 axons (tibialis anterior: 689 axons; extensor digitorum longus; 429 axons; flexor hallucis longus: 695 axons) having conduction velocities ranging from 50 to 106 m/sec, the stimulation of 1793 axons elicited the contraction of extrafusal muscle

The remaining 20 axons were probably damaged during the dissection of the nerve near its entry in the muscle since their repetitive stimulation did not elicit either a muscle action potential or spindle discharges.

SPECIFIC CHOLINERGIC VASODILATATION IN CONTRACTING LIMBS DURING CONDITIONED MOVEMENTS. G.D. Ellison and A. Zanchetti. Cardiovascular Res. Inst., Univ. of Milan, and Cardiovascular Res. Ctr., CNR, Milan, Italy.

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Cats were trained with a 500 Hz tone signalling the coming, 5 sec later, of a brief shock to a hind limb. Animals which learned a relatively specific unilateral leg flexion response (upon presentation of the tone) were implanted with electromagnetic flow probes on both external iliac arteries, and with a blood pressure cannula. On trials when no conditioned flexion occurred, there was statistically significant (p < 0.01) vasoconstriction in both limbs. On the other hand, on trials in which the animals showed a specific conditioned flexion response of only the trained limb, only the contralateral immobile limb showed the usual vasoconstriction: in the trained contracting limb there was statistically significant (p < 0.01) vasodilatation. Disappearance of this vasodilatation after administration of methylatropine (0.5 mg/kg i.v.) indicated that it was mediated cholinergically. The observation that cholinergic vasodilatation appears only when conditioned movements occur and only in the responding leg, demonstrates that the sympathetic cholinergic system supplying muscle blood vessels can exert a highly specific and motor-related action.

TEMPERATURE REGULATION OF NEWBORN WEDDELL SEALS <u>LEPTONYCHOTES WEDDELLI</u>. <u>R. Elsner</u>, <u>D. D. Hammond</u>, <u>D. M. Denison</u>, and <u>C. J. Farwell</u>. Scripps Institution of Oceanography, <u>University of California at San Diego</u>, <u>La Jolla</u>, California 92037, USA. Weddell seal pups were studied at McMurdo Sound, Antarctica. Birth takes place on

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Weddell seal pups were studied at McMurdo Sound, Antarctica. Birth takes place on the sea ice, and pups usually do not venture into the water until two weeks of age. Continuous direct contact with the ice is unavoidable, and little maternal sheltering is possible. Field observations were made of meteorological conditions and rectal temperature (Tr) and behavior of infant animals in the seal colony. Lanugo fur required two to three hours after birth to dry and become effective insulation. Birthweight averaged 30 kgs. Weight increased about 2.5 kgs. per day. Subcutaneous fat was meager at birth but rapidly increased in thickness. Histological examination of mature fetal tissues failed to reveal brown fat. Tr was maintained during air exposure. However, when newborn seals were immersed in sea water (-1.8°C) Tr fell rapidly, and shivering occurred. By the tenth day immersed pups maintained Tr without shivering. Five newborn animals were studied experimentally during the first four weeks of life. Oxygen consumption (VO_2) and Tr were recorded during quiet, apparently basal, two-hour periods in a metabolic chamber at -15°C (approximate mean temperature in the seal colony during the study). VO_2 averaged 6.8 ml/kg/min. As in other seals this value is higher than in terrestrial mammals of similar weight. RQ averaged 0.76, reflecting the high fat content of Weddell seal milk. Insulative protection was provided in the first days of life by fur, later by subcutaneous fat. (Supported by Grant GV-23899 from the NSF Office of Polar Programs.)

- LOCAL EFFECTS OF ACID INFUSION ON GRACILIS MUSCLE VASCULAR RESISTANCE. T. E. Emerson, Jr. and G. W. Jelks. Dept. of Physiol., Mich. State Univ., East Lansing, Mich., U.S.A. 472 reported previously that in the dog gracilis muscle, locally increasing blood pH from 7.47 to 7.67 by i.a. alkali infusion did not alter vascular resistance, but that further increases in pH with NaOH or Na₂CO₃ caused striking increases in resistance (Fed. Proc. 28:519, 1969). In the present study, isotonic solutions of acetic (N=15) or lactic (N=17) acid were infused locally at sequentially faster rates in constant flow perfused, innervated, isolated gracilis muscles. Saline was infused as a volume control. Decreasing blood pH with acetic acid from an average of 7.42 to 7.22 resulted in a progressive decrease in perfusion pressure and muscle vascular resistance; the greatest fall in resistance occurred during the first pH reduction (-0.03 units). Decreasing pH below 7.0 consistently resulted in a marked increase in resistance. Neither systemic arterial pressure nor blood pH changed appreciably during the infusion. Vascular resistance returned to near control level when the acid infusion was discontinued and muscle pH returned to control. Changes in pH, perfusion pressure and vascular resistance were similar during infusion of lactic acid. The decrease in resistance during local reduction of blood pH appears to result from an active change in vessel caliber; the increase in resistance which occurs at extremely low pH's may be related to a change in blood viscosity. These data support the hypothesis that the H⁺ may play a role in local regulation of blood flow since venous blood pH is slightly reduced in skeletal muscle during active or reactive hyperemia (supported by NIH grant HE-10899).
 - RAPID pH-CHANGES AND THE MOLECULAR ARRANGEMENT OF RETINENE AND PHOSPHATI-473 DYLETHANOLAMINE IN ROD OUTER SEGMENTS DURING RHODOPSINPHOTOLYSIS. H.M. Emrich. Max Volmer Institute, I. Institute of Physical Chemistry, Technical University of Berlin, West-Berlin.

Using pH-indicators in flash-absorption-photometry of isolated bovine rod outer segments a rapid alkalization is observed which runs parallel to the metarhodopsin I-II decay. On this reaction two hypotheses have been proposed: 1. The cleavage of a Schiff-base-bond of retinal with phosphatidylethanolamine (PE) (Poincelot et al. (1)). 2. The release of a imidazole-group of histidine (Matthews et al. (2)). Our experiments favour the assumption of a cleavage of a Schiff-base compound during the metarhodopsin I-II reaction and indicate that this reaction causes the spectral change as well as the pH-change. Furthermore X-ray experiments demonstrate that retinene combinds with PE in a special conformation as a mixing micelle (30 A) in which a Schiff-base bond is proved spectroscopically. (1) Nature 221, 256 (1969) (2) J.Gen.Physiol. 47, 215 (1963).

- INTRACELLULAR RECORDING OF MEMBRANE POTENTIAL IN THE NEWT RED CELLS. A. Endo, M. Fukushima, 474 C. Ibuki and K. Kawaguchi. First Department of Physiology, Nippon Medical School, Tokyo, Japan.

Measurements were made on the transmembrane potentials of newt nucleated erythrocytes to know the effect of several external ions. The microelectrode was advanced simply with a micromanipulator and the potential change was photographed continuously during the course of impalement. Mean value of the membrane potentials examined in Ringer fluid was -15.2 ± 0.1 mV with a range of -6.7 - -31.7 mV (133 observations), as against the maximum value of -14 mV observed by Lassen and Sten-Knudsen (1968, J.Physiol.) on human red cells. High chloride (166 mM) Ringer increased the magnitude of potential by about 9 mV and high calcium (18 mM) Ringer by about 4 mV. The specific membrane resistance was also measured. INHIBITION OF ANGIOTENSIN-CONVERTING ENZYME IN VIVO BY PEPTIDES FROM SNAKE VENOM.
S.L. Engel, T.R. Schaeffer, B.I. Gold, and B. Rubin. Squibb Inst. for Med. Res., New Brunswick, N. J., U.S.A.

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Extracts of venom from Bothrops jararaca have been reported to exhibit two activities in vitro and in vivo, potentiation of the effects of bradykinin and inhibition of the conversion of angiotensin I to angiotensin II. Seven peptides isolated from B. jararaca venom and then synthesized by M. Ondetti et al. were administered by rapid i.v. injection into urethanized rats pretreated with atropine sulfate and heparin and infused with pentolinium bitartrate in tests for inhibition of pressor responses to angiotensins I and II and for effects on "resting" blood pressure. The compounds, in decreasing order of potency in terms of both degree and persistence of inhibition of angiotensin I-induced pressor responses, are as follows: Pyr-Asn-Trp-Pro-His-Pro-Gln-IIe-Pro-Pro> Pyr-Trp-Pro-Arg-Pro-Gln-IIe-Pro-Pro> Pyr-Trp-Pro-Arg-Pro-Gly-IIe-Pro-Pro> Pyr-Gly-Gly-Trp-Pro-Arg-Pro-Gly-IIe-Pro-Pro> Pyr-Gly-Gly-Trp-Pro-Arg-Pro-Gly-Pro-Glu-IIe-Pro-Pro> Pyr-Ser-Trp-Pro-Gly-IIe-Pro-Pro> Pyr-Gly-Gly-Trp-Pro-Arg-Pro-Gly-Pro-Glu-IIe-Pro-Pro> Pyr-Ser-Trp-Pro-Gly-Pro-Asn-IIe-Pro-Pro> Pyr-Iys-Trp-Ala-Pro. No significant inhibition of the pressor responses to angiotensin II was noted. Thus, these synthetic peptides derived from B. jararaca venom are active in vivo as presumptive inhibitors of the angiotensin-converting enzyme.

FACILITATED TRANSPORT OF CARBON MONOXIDE AND OXYGEN BY MYOGLOBIN AND HEMOGLOBIN IN INTACT CELLS. T. Enns. Scripps Institution of Oceanography, University of California, La Jolla, California U.S.A.

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The diffusion transport of carbon monoxide through slices of myoglobin rich buccal muscle of the sea slug Aplysia californica is greater than that through water, but is reduced by potassium ferricyanide. Similar transport changes are obtained in human blood and erythocyte suspensions. Furthermore carbon monoxide transport is reduced in the presence of oxygen, indicating that facilitated oxygen transport replaces facilitated carbon monoxide transport. These data are compatible with the concept that myoglobin and hemoglobin facilitate carbon monoxide and oxygen transport inside intact cells.

METABOLIC INHIBITORS ON ELECTRICAL PROPERTIES OF CRAB MUSCLE FIBERS.R. Epstein and M.A. Hardy(Jr)Centro de Invest. Neurológicas.Inst. T. Di Tella. Buenos Aires, Argentina.

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The effects of 2,4-dinitrophenol(.4 mM at pH 6.5), sodium azide (4 mM) and low temperature on the effective resistance (Reff) of different types of crab muscle fibers were studied. Dinitrophenol (DNP) produces an increase in Reff which is more marked in thin fibers(70-100% increase) than in thick fibers (20-50% increase) at resting potential levels. Sodium azide on the contrary has a variable and small effect on Reff, but if fibers are pretreated with NaN3, no effect is seen on addition of DNP. A similar blockage of the DNP effect was obtained if the preparation was cooled below 109C before adding DNP to the medium. Cooling by itself augmented Reff.

It is supposed that these observations indicate linkage between the energy metabolism and membra ne conductance in accordance with the high Q10 of the membrane resistance which has been observed in muscle fibers of other crab species.

ANALYSIS OF REFLEX CONTRACTIONS OF THE NICTITATING MEMBRANE IN CATS.

A.Erdélyi, Izabella Morava, G.Pavlik and A.Mitsányi. Dept.of Experimental Physiology, State Inst.of Occupational Health, Budapest, Hungary.

Experiments were performed on non-anaesthetized cats, and on cats anaesthetized with chloralose-urethane, both groups under artificial respiration and immobilized by gallamine. Reflex contractions of the nictitating membrane, elicited by square wave stimulation of the sciatic nerve, with parameters varied over a wide range, were analysed. The magnitude of the contractions was found to display a characteristic dependence upon the parameters of stimulation. Evaluation of this dependence indicates a possible difference between the central representation of the vasomotor system, and the neurons activating the nictitating membrane. It is suggested by the data that the two systems might have common representation on higher levels of the CNS, whereas the nictitating membrane does not seem to be represented in the lower centres playing an important role in the regulation of the peripheral vascular tone.

METABOLISM OF VASOACTIVE PEPTIDES BY A LUNG ENZYME. E.G. Erdős, R. Igic, H.S.J. Yeh, T. Seki. Dept. of Pharmacol., Univ. of Oklahoma, Oklahoma City, U.S.A.

The conversion of (Aspl-Ile⁵_14c Leu¹⁰) angiotensin (Ang) I to Ang II was studied in the perfused rat lung. The converting enzyme (dipeptide hydrolase) cleaved His⁹_14c_Leu¹⁰ from Ang I. The dipeptide split product was isolated from the lung effluent by means of thin-layer chromatography. The reaction was inhibited by bradykinin, glutathione, EDTA and by the peptide SQ 20881. In addition to the lung, the enzyme occurs in a microsomal fraction of the homogenized kidney cortex and in blood plasma. The highest concentration in blood was found in the guinea pig. The enzyme was extracted from homogenized swine lung and partially purified. It was subsequently bound to a water insoluble carrier Sepharose 4B. The insoluble Sepharose-enzyme complex was placed into columns and solutions of peptides were passed through the columns. Ang I was converted to Ang II and bradykinin was inactivated during passage. The experiments support our previous studies that the two peptides, bradykinin and Ang I, are metabolized by the same enzyme (converting enzyme or kininase II) which cleaves C-terminal dipeptides from hypertensive and hypotensive peptide substrates. (Supported by USPHS, HE 08764 and by ONR NO0014-68-A-0496)

480 MYOCARDIAL OXYGEN CONSUMPTION DURING HYPOXIC HYPOXIA. H.H. Erickson (Stone). Applied Physiology Branch, USAF School of Aerospace Medicine, Brooks Air Force Base, Texas 78235, U.S.A.

The relative importance of B-adrenergic receptors in the cardiac response to hypoxia was investigated in 19 conscious dogs. A Doppler ultrasonic flow transducer was placed around the left circumflex coronary artery and a solid-state pressure transducer in the apex of the left ventricle. Catheters were placed in the left atrium and coronary sinus in order to determine blood gases and pH of arterial and coronary venous blood. The A-V difference in oxygen content across the heart and the oxygen consumption of the left ventricle were calculated at rest and during hypoxia in 7 dogs. Gas mixtures, consisting of 10% or 5% oxygen in nitrogen were breathed through an endotracheal tube inserted in a permanent tracheostomy. Hypoxia (5% oxygen) caused the heart rate to increase from 87 to 113 b/m; after B-blockade it increased from 78 to 92 b/m. Maximum left ventricular dP/dt increased from 3335 to 4586 mm Hg/sec, while after B-blockade it only increased from 2818 to 3431 mm Hg/sec. The increase in heart rate, dP/dt, and the decrease in the A-V difference in oxygen caused the coronary flow to increase from 44 to 103 ml/min; after B-blockade it only increased from 41 to 85 ml/min. Hypoxia resulted in an increase in left ventricular oxygen consumption from 4.4 to 6.7 ml/min, while after B-blockade it only increased from 3.7 to 4.4 ml/min. These results indicate that B-adrenergic receptor activity in the myocardium participates in the integrated response to hypoxia; however, active dilation of the coronary vessels does not seem to occur.

FUNCTIONAL SIGNIFICANCE OF THE CONNECTIONS OF SUPERIOR COLLICULUS. Alfonso Escobar Dept. of Neurobiology, Inst. Investigaciones Biomédicas, Univ. Nac. Autón. México. Ciudad Universitaria, México 20, D.F., MEXICO

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Visual information constitutes one of the most important sources for motor coordination in higher mammals. The superior colliculus maintains a complex structure in the animal scale. From our own studies new connections from superior colliculus to the brainstem and hemispheric structures have been established in ten cat brains by means of unilateral ablation of the superior colliculus and anatomical study using the Nauta and Marchi techniques. The results show the existence of a well defined descending connection to the n. Beta of the inferior olivary complex; this bundle id evident only with the Nauta impregnation. Other descending connections agree with those previously described by others. Among the ascending connections one not hitherto described is that to the ipsilateral thalamic centromedian nucleus as well as one to the lateral hypothalamic area. A fundamental observation from studies of the unitary physiology of the cerebellar cortex is the dual input to the cerebellar cortex, one via the mossy fiber and the other via the climbing fiber. This superior collicular - inferior olive - cerebellar connection provides the climbing fiber input to match the mossy fiber input from the superior colliculus via the pontine nuclei. The superior collicular - centromedian nucleus connections adds another path to intervene in visuo - motor coordination.

BLOCK OF CONDUCTION OF INTRASPINAL BRANCHES OF PRIMARY AFFERENT FIBERS BY CARBON DIOXIDE. Don W. Esplin, R. Capek and Barbara Zablocka-Esplin. Department of Pharmacology and Therapeutics, McGill University, Montreal, Canada.

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The quantal release of transmitter in the spinal monosynaptic pathway was studied in unanesthetized spinal cats. Synaptic potentials were recorded intracellularly from motoneurons activated monosynaptically by peripheral stimulation of a single group Ia afferent fiber. Responses were studied after at least 5 minutes exposure to a mixture of 10 to 20% CO2. A control series of approximately 200 synaptic potentials was distributed as predicted by the Poisson probability function, and the number of failures was in accordance with the calculated mean quantum content. However, after exposure to CO2 there was a disproportionate increase in the number of failures, but the distribution of potentials when release occurred was similar to that in the control series. This indicates that the extra failures were due to failure of impulse conduction between the point of dorsal root recording and the motoneuron. The amplitude of the potential produced by one quantum of transmitter was not appreciably affected by CO_2 . The gas had variable effects upon the motoneuron. It generally produced a slight but reversible depolarization, and membrane resistance was usually somewhat decreased. The excitability of the motoneuron to orthodromic, antidromic, or intracellular stimulation was sometimes increased and sometimes decreased. (Supported by the Medical Research Council of Canada.)

INFLUENCE OF CYCLIC-AMP ON THE PASSIVE PERMEABILITY OF NON-ELECTROLYTES THROUGH THE INTESTINAL WALL. G. Esposito, A. Faelli, G. Garotta and V. Capraro. Institute of General Physiology, University of Milan, Milan(Italy)

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In the everted jejunal sac of rat, the addition of glucose (14 mM) to the perfusion fluid lowers in a significant way the electrical resistance of the intestinal wall and increases the passive permeability to non-electrolytes (acetamide).

As previously demonstrated, such an increase of permeability is not due

to a cellular swelling of the epithelial layer.

The hypothesis is put forward that the increased permeability could be related to an higher intracellular concentration of cyclic-AMP, when glucose is present in the incubating medium.

This view is supported by the fact that the passive permeability to non-electrolytes is increased by the cyclic-AMP added to the incubating

medium.

484 ELECTRICAL ACTIVITY OF RETINAL FIBERS AFFERENT TO THE OPTIC TECTUM IN THE TELEOST Eugerres plumieri. E. Essayag-Millán, H. Vanegas and M. Laufer.

Dept. Neurobiology, IVIC, Caracas, Venezuela
Stimulation of the postral end of the optic nerve with single shocks gives rise to a sequence of six waves in the contralateral optic tectum. The first three of these (waves 1, 2 and 3) are herein shown to correspond to activity in optic nerve fibers. Surface recordings of compound action potentials in optic nerve or tract show three negative waves (I, II and III) with conduction velocities similar to those calculated for waves 1, 2 and 3, namely, 20, 10 and 6 m/s, respectively. The 20 m/s group had not previously been reported in fish or amphibians. When a semimicroelectrode is introduced step wise in a direction perpendicular to the optic fiber layer of the tectum, waves 1, 2 and 3 remain negative in polarity throughout the tectal thickness. Finally, in recordings made from the tectum by means of micropipettes or plat inum microelectrodes, waves 1, 2 and 3 coincide only with unitary spikes which: a) have a 1:1 relationship with suprathreshold stimuli; b) follow stimulus frequencies of 50 to 100 per second, whereas units which coincide with other waves cannot follow stimulus frequencies higher than 10 per second; c) have constant latencies even at high frequency stimulation; and d) are encountered only at depths of 220 to 360 µm from the tectal surface, i.e. coincident with the range of distribution of incoming optic nerve fibers.

RETROGRADE AMNESIA AND CEREBRAL PROTEIN SYNTHESIS: INFLUENCE OF AGE AND DRUG FACTORS.

W. B. Essman. Departments of Psychology and Biochemistry, Queens College of the City University of New York.

In mice a retrograde amnesia for passive and active avoidance behavior has been produced by electroconvulsive shock (ECS) temporally proximal with training. This effect is paralleled by a (1) rise in brain 5-hydroxytryptamine (5-HT) level, peaking at 10 min. post-shock; (2) reduced RNA levels associated with synaptosomes and mitochondria from cerebral cortex; (3) inhibition of brain protein synthesis (4 to 42%) with diminishing effect lasting as long as 60 min. post-shock; and (4) regional inhibition of protein synthesis, maximal in the basal ganglia and diencephalon by 5 min. following ECS (60%), where synaptoscmal protein synthesis was inhibited by 41%. Intracranial 5-HT treatment led to a retrograde amnesia as a function of age, training-injection time, and drug treatment; 17 day old mice, showing higher rates of cerebral protein synthesis and lower endogenous 5-HT levels than younger or older animals, were maximally resistant to the amnesic effects of 5-HT, and showed reduced inhibition of regional brain protein synthe-The effects of nicotine and its active metabolites in adult mice attenuated the amnesic effects of (1) ECS by blocking brain 5-HT elevation and (2) 5-HT by reduction of its storage; in both instances regional and sub-cellular protein synthesis inhibition was also modified by nicotine and those metabolites which attenuated the amnesic effect. (Supported, in part by grant HD-03493 from the N.I.H. and a grant from the Council for Tobacco Research-U.S.A.)

486 EFFECTS OF ETHANOL IN NEURO-MUSCULAR CONTRACTION.S. Etessami. Dept. of Physiology, Univ. of Teheran, Faculty of Med. IRAN.

We can find many studies about ethanol concerning his effects in: central nervous systeme, blood dosage, metabolic activity, respiratory tract, etc, but we can not find some explication of ethanol activity in neuro-muscular conductivity and excitability. This work is reserved for those studies, we observed that: 1-The effect of higher doses of ethanol in isolated neuro-muscular preparation is a blockade conduction, this blockade seems to be caused by some instable depolarization.2-Low concentration of ethanol increases the excitability of the celle and in high concentrations decreases or abolishes this excitability. 3-With ethanol low concentrations the nerve repolarizes spontaneously, but the depolarization activity caused by ethanol high concentration, produce a blockade of conductivity, in this case the contraction can recover after reestabilisation of the membrane potential, by an external anodic current.4-Addition of a low concentration of prostigmine before administration of a low ethanol concentration in bath organ, can induce some facility for blockade production, and we are observed like Barnes and collaborators, that, alcohol in high cencentration inhibits the cholinestérase activity.5-If we expose a motor frog nerve in some ethanol solution with different concentration, we can see that the decrease of membrane potential is proportion to the alcohol concentration.

Does Frequency Sharpening Occur in the Cochlea? <u>E.F. Evans</u>. M.R.C. Group, Department of Communication, University of Keele, Keele, Staffs, U.K.

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(1) Our own data from single cochlear nerve fibres in the cat confirm those of Kiang et al. (1967, J. acoust. Soc. Am. 42: 1341), and indicate that the effective bandwidth of the frequency response curves are between 3 and 5 times narrower than the analogous resonance curves derived for the basilar membrane by von Bekesy (e.g. 1944, Akust.Z. 9:3) and Johnstone & Boyle (1967, Science, 158: 389). (2) However, objection may be raised to this on the grounds that no mechanical data exist for the cat, and that measurements by Tasaki (1954, J. Neurophys. 17:97) on the guinea pig cochlear nerve responses are similar to the mechanical response curves of that species. The cochlear nerve experiments in the guinea pig have therefore been repeated using an intracranial approach to the cochlear nerve and a calibrated closed sound field. The response curves obtained are at least as narrow as those from the cat, and the boundaries significantly steeper than in the appropriate mechanical curves. (3) The simplest explanation for the above is that the surgical techniques required to measure the motion of the basilar membrane deprive it of sharply 'tuned' properties. Experiments to test this in the guinea pig show that the narrow frequency response curves can still be obtained from cochlear nerves when the sc. tympani is opened and the local perilymph drained, as when measurements of the mechanical response are made. It therefore appears that either the mechanical measurements are in error or the cochlea contains a further frequency selective mechanism in addition to that derived from the vibration pattern of the basilar membrane.

NEURAL BASIS OF VISUAL BEHAVIOUR IN TOADS
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How does the toad's visual system encode essential characteristics of small prey-like or large enemy-like objects? (1) Extracellular recording studies indicate that the retinal ganglion cells transmit to the brain first-order classifications of visual stimuli (angular velocity, angular size, contrast with the background) that seem necessary but not sufficient for identification of prey and enemy objects. (2) It seems likely that the caudal thalamic (T) and pretectal (P) structures play a role in modulating prey-catching and avoiding tendencies. TP-units are activated mainly by large enemy objects such as a black 40° disc moved through the excitatory receptive field (ERF); small 2° prey objects are not effective. The ERF (30°) of these units can expand to 50° and also change the shape. (3) Focal electrical stimulation of the TP-region in free-moving toads leads to avoidance reactions such as ducking, turning away or jumping. (4) After destroying caudal thalamic and pretectal structures by high frequency coagulation the visual escape behaviour fails and the prey-catching behaviour is hyperexcited even to large enemy objects.

INTERACTION OF STRYCHNINE WITH ACETYLCHOLINE AND DOPAMINE RECEPTORS IN APLYSIA NEURONS. D.S. Faber, M.R. Klee and W.D. Heiss, Neurosensory Lab., Dept. Physiol., SUNYAB, Buffalo, N.Y., USA, and Max-Planck-Inst. Hirnforschung, Neurobiol. Abt., Frankfurt-M., Germany.

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Strychnine in concentration of 1mM in the bathing medium blocks all excitatory and most inhibitory post-synaptic potentials. Also, axonal threshold increases and conduction velocity decreases, resulting in blockage of antidromic invasion. To determine whether the reduction of PSP amplitudes was due to a pre— or postsynaptic action, we studied the effects of different concentrations of strychnine (0.01-2.5 MM) on the Responses of identified neurons to iontophoretic application of acetylcholine (ACh) and dopamine (DOP). Depolarizing (D) responses to both ACh and DOP were reduced, the DOP-D responses being the most sensitive to strychnine. The dose-response curves (DRC) for ACh-D cells were parallel and shifted to the right, maximally by 1 log unit. The competitive inhibition of ACh-D responses by strychnine is similar to that of curare (dTC), which was 10 times more effective on these responses. Hyperpolarizing (H) responses to DOP were also reduced, but much less so; the DOP-H DRC were shifted to the right by at most 0.3-0.5 log units. The DRC of ACh-H responses were shifted to the left, especially in cells L2-L6. Similar increases in amplitude have been reported for dTC and hexamethonium, upholding the known curare-like action of strychnine. Agonistic actions of strychnine and eserine were often observed in these cells. We have confirmed that TEA (o.1mg/ml) blocks these ACh-H responses; however, copper sulfate (o.1mg/ml) also completely blocks them, raising doubt as to their genesis by potassium conductance changes alone.

490 CARDIOVASCULAR HOMEOSTASIS BEFORE BIRTH. J. Job Faber, Lawrence R. Long and Thomas J. Green. Department of Physiology, University of Oregon Medical School, Portland, Oregon, 97201, U.S.A.

The heart of the vertebrate embryo reacts to an increase in filling pressure with an increase in strength of contraction. Stroke volume is thus dependent on blood volume, even in the earliest days of the functional existence of the heart before autonomic innervation takes place. Blood volume depends on the osmotic and hydrostatic pressures of the plasma in the extra embryonic capillaries and those of the extra embryonic fluid volumes with which the plasma equilibrates. It would appear that a simple equilibrium of the Starling-Landis type in the extra embryonic capillaries, together with a regulated embryonic plasma protein level and the Frank-Starling mechanism of the heart can account for the long term regulation of embryonic blood volume and flow. These views are explored by experiments on water exchange between embryonic and extra embryonic fluid compartments, measurements of cardiac output as a function of blood volume, and osmotic water shifts in the prenatal chicken and sheep.

Supported by NIH grants HD2313 and HE13444, MRF of Oregon 23.01, and an Established Investigatorship of the American Heart Association.

JUNCTIONAL ACTION POTENTIALS IN HUMAN ATRIAL MUSCLE. A. Fabiato & F. Fabiato Physiologie Comparée (Pr E. Coraboeuf), Faculté Sciences, Orsay, France.

Various degrees of dissociation were demonstrated in the action potential of human atrial strips: 1) notch between initial spike and "dome-shaped" slow phase, 2) two components separated by a low "plateau", 3) occasional disappearance of one of the two components ("two to one" block or "Wenckebach-like" phenomenon), 4) either total disappearance of one of the two components or appearance of multiple components. Transformation from 1) to 4) was elicited by factors of non-homogeneous activation including: lowering temperature, lowering intensity of stimulation, increasing frequency, high K⁺, low Ca⁺⁺or hypertonic solutions, tetrodotoxine.Non-homogeneous activation was further demonstrated by simultaneous recordings with two microelectrodes. Variability of one of the components (generally the initial spike) suggests that it might be due to the electrotonic propagation of the activity of tissues surrounding the explored cell; while the larger and less variable component (generally the second one) would be the proper activity of this cell. Each electrical component was accompanied by a mechanical event; in contrast to this non-homogeneous response in a multicellular strip, contraction of single human atrial cells (dispersed by enzymes) never exhibited several components.

PREGNENOLONE AND PROGESTERONE SECRETION BY PMS-HCG STIMULATED OVARIES OF THE SQUIRREL MONKEY. A. B. Fajer, Dept. of Physiol., Sch. of Med., Univ. of Maryland, Baltimore, Md. U.S.A.

Sexually immature animals (Saimiri sciureus) were made to ovulate with PMS-HCG administered during a 9 day treatment. Extensive follicular growth did not permit the diagnosis of ovulation without histological examination of the ovaries. Ovulation is followed by extensive luteinization. Pregnenolone (0.30 $\mu g/ml$) and progesterone (0.77 $\mu g/ml$) can be detected in the ovarian venous blood of all animals two days after ovulation but only in 50% of the animals and in lower concentration five days after ovulation. The interstitial tissue is suggested as the possible source of pregnenolone in this species. (Supported in part by a grant from the National Science Foundation, USA.)

ON THE NEURONAL ORGANIZATION OF THE CEREBELIAR NUCLEI.V.V.Fanardjian,A.S. Amatuni,E.A.Ohanessian. Orbeli Inst. of Physiology,Armenian Academy of Sciences, Yerevan, USSR.

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The activity of the cerebellar subcortical neurones on their antidromic and synaptic excitation by stimulating brain stem nuclei, sensorimotor cortex and peripheral nerves was investigated in cats under nembutal anaes thesia. Several functionally different groups of neurones were distinguished. Thus, in nucleus dentatus there had been reveald the following four groups: efferent neurones antidromically activated from brain stem nuclei, which did not respond to peripheral nerve stimulation(I); neurones synaptically activated from brain stem nuclei and responding in most cases to peripheral nerves and cerebral cortex stimulation(II); cells with background rhythmical activity not responding to any kind of stimulation applied(III) neurones having characteristics of interneurones responding selectively to certain peripheral nerve stimulations or with large convergency of influences from various afferent sources. It was also discovered that not all nuclear neurones were under influence of cerebellar cortex. Alongside with that there were found regions with maximal density of projections from cerebellar cortex to central nuclei corresponding to three longitudinal cortico-nuclear zones revealed morphologically.

THE INFLUENCE OF PROLONGED STARVATION ON THE FREQUENCY OF OCCURRENCE OF DECOMPRESSION-INDUCED PULMONARY HEMORRHAGE. H. S. Fang and H. S. Lin. Departments of Physiology and Anatomy, Natl. Taiwan University College of Medicine, Taipei, Taiwan, Republic of China.

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The lungs of toads were very tolerable for explosive decompression. The tolerance of such laboratory amphibia to explosive decompression from one atmospheric pressure (760 mmHg) to an ambient pressure of 54 mmHg in 0.04 seconds was markedly reduced when the animals were previously subjected to prolonged starvation for 257 to 271 days. The frequency of occurrence of decompression-induced pulmonary hemorrhage in control and prolonged starved animals was 10% and 50%, respectively. In 2 of the 20 starved animals, both lateral body walls were ruptured because of sudden rapid overexpansion of the gas-containing hollow organs following explosive decompression. The average dry lung weight of starved animals was 30.5 mg, while the value for the control group was 54.9 mg. The difference was statistically significant. It was also observed that the smooth muscle fibers in the alveolar septa as well as in the pulmonary vessels were markedly atrophied after prolonged starvation. Such an atrophy of smooth muscle fibers and possibly other pulmonary tissue might reduce the resistance of lungs to explosive decompression resulting in an increase of incidence of pulmonary hemorrhage.

THE ROLE OF CHOLECYSTOKININ AND SECRETIN IN THE MESENTERIC VASCULAR RESPONSE TO INTRA-DUODENAL FAT AND ACID. J.W. Fara, E.H. Rubinstein, and R.R. Sonnenschein. Dept. of Physiology, UCLA School of Medicine, Los Angeles, Calif. 90024 U.S.A.

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The instillation of 1.5 ml fat (corn oil) or 0.127 M L-phenylalanine (0.1-0.2 cc/min) directly into the duodenum of chloralose-anesthetized cats produced a 20-50% increase in superior mesenteric blood flow (blocked by atropine), with a 3-12 min latency and 45-90 min duration, which was accompanied by an increase in gall bladder and duodenal motility and pancreatic enzyme output. This response could be mimicked by the intravenous infusion of 0.6-3.5 units/kg/hr cholecystokinin (CCK). The intraduodenal infusion of 0.127 M hydrochloric acid (0.5-1.5 cc/min) produced a similar superior mesenteric vasodilatation and an increase in bile and pancreatic volume outputs which could be mimicked by the intravenous infusion of 1.5-4.0 units/kg/hr secretin. The intravenous infusion of CCK or secretin failed to elicit blood flow changes in the renal, femoral, gastric or large intestinal vascular beds, but did increase pancreatic and small intestinal blood flows by equal amounts. The vasodilatation in the pancreas and small intestine following intraduodenal fat or L-phenylalanine and intravenous CCK or secretin was accompanied by an increased oxygen consumption of these tissues. It is concluded that the duodenal hormones cholecystokinin and secretin play a physiological role in the mesenteric vascular response following intraduodenal fat or acid. Supported by grants from USPHS (NE-05157 & HE-5696), Amer. Heart Assn. (69880 & 69127), and Los Angeles County Heart Assn. (4371G).

496 MANIFESTATIONS AND MECHANISMS OF MOTOR FATIGUE IN MAN. V.S.Farfel and Y.M.Kots. Central Inst., of Physical Culture, Moscow, USSR

A study of the reflex excitability and impulse activity of the motoneurons of the gastrochemius muscles shows that local work gradually involves new, more high-threshold motor units of the working muscles.Registration of the electrical and mechanical responses of the muscles to a tetanic stimulation of their nerve reveals a gradual decrease in both responses during work to the point of fatigue. Hence it was concluded that the recruiting of new motor units compensates for the gradual decrease in the force of contraction of the working units resulting from fatigue. Fatigue in total muscle work was studied by means of recording the changes in the rate of movement, frequency of movements and the length of strides in long distance running, walking, swimming and skating competition. The fatigue manifested itself mainly in shortened strides and arm pulls, which resulted in lowered speed. Fatigue is also accompanied by an increased support period in running and a decreased period of double support in walking. All this indicates a decrease in the power of contraction of the basic working muscles. It is possible that also in this case, as in local work, the observed phenomena are a result of fatigue of the peripheral neuromuscular apparatus.

497 LACK OF RESPONSE TO L.H. DURING DIABETES IN THE RAT. Farina, J.M.S.; Chieri, R.A.; Basabe, J.C.; Foglia, V.G. Institute of Physiology, Buenos Aires University, Argentine.

The present investigation was designed to study the ovarian sensitivity to exogenous gonadotrophins during diabetes in the rat, as measured by the ovarian cholesterol depletion induced by L.H. In the normal rat the total ovarian cholesterol is 1267 $^{\pm}$ 70 (n=9) corresponding 428 $^{\pm}$ 27 (n=9) to free cholesterol and 840 $^{\pm}$ 82 (n=9) to sterified cholesterol ($\bar{\chi}$ $^{\pm}$ se; mg/100 g ovarian wet weight). L.H. injections decreases the cholesterol levels to:total 629 $^{\pm}$ 49 (n=8); free 331 $^{\pm}$ 27 (n=8); sterified 316 $^{\pm}$ 40 (n=8). Cholesterol levels in the partial pancreatectomized diabetic rats were: total 1166 $^{\pm}$ 79 (n=12); free 402 $^{\pm}$ 26 (n=9) sterified 700 $^{\pm}$ 55 (n=12).L.H. Injection to the partial pancreatectomized rats did not modified the cholesterol levels. The following results were obtained. Total 1070 $^{\pm}$ 68 (n=14); free 351 $^{\pm}$ 16 (n=12). Sterified 745 $^{\pm}$ 78 (n=14). Aloxan diabetic rats showed the same lack of response to the exogenous L.H. injection. Insulin treatment to the diabetic animals restores the ovarian sensitivity to the gonadotrophin injection.

AGE DEPENDENT CHANGES IN THERMOREGULATION IN THE RATS. Maria Farkas. Dept. of Pathophysiology, Univ. Med. Sch., Pécs, Hungary.

Body temperature /BT/ and 0_2 -consumption were measured at environmental temperatures of 35°C, 20°C and 10°C in rats aged 1, 2, 6, 12, 18, 24 and 28-30 months. At 20°C, the response to 12 % 0_2 and to 6 % CO $_2$ was also observed. 0_2 -consumption and BT were measured continuously with a Noyons-Kipp diaferometer and cupper-constantan thermocouples respectively. In response to 35°C environmental temperature the increase in BT and in 0_2 -consumption was greatest in the youngest age-group. At 10°C, the decrease in BT was greatest in the oldest and in the youngest age-groups, the increase in 0_2 -consumption decreased with age. In response to 12 % 0_2 or 6 % CO $_2$ the decrease in BT and in 0_2 -consumption increased with age. I.v.pyrogen /E. coli lipopolysaccharide/ was followed by hyperthermia regularly in young rats but only about 0_2 of the old rats. The changes in response of BT and 0_2 -consumption in old rats are not due to simple deterioration of the effector mechanism, but to changes in the central regulating mechanism resembling in many aspects those observed in the youngest animals.

KINETIC EVALUATION OF NA REQUIREMENT FOR THE INTESTINAL ABSORPTION OF D-GLUCOSE IN FREE SWIMMING FISH. A. Farmanfarmaian. Marine Biol. Lab., Woods Hole, Mass. and Dept. of Physiology, Rutgers Univ., New Brunswick, N.J., U.S.A.

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The mucosal requirement of Na for the in vitro accumulation transport of sugars and amino acids by the intestinal epithelium of mammals have been reported by many authors. More recently several investigators have indicated that substrate uptake is not affected by mucosal Na but by intracellular changes of Na caused by the serosal concentration of Na under in vitro conditions. We have subjected this problem to kinetic analysis of Na glucose interactions in the intestine of the toadfish, <code>Opsanus tau</code> under free swimming conditions. It was shown that glucose is absorbed against a gradient, and that 10^{-4} M phloridzin inhibits more than 95% of this transport both at 1.0 and 10.0 mM initial glucose concentration in normal saline. When mucosal Na was reduced nearly 10 fold by substitution of choline, Tris or K the changes in K, were not significant (P<0.05). The changes in V were significant (P<0.05) only in the case of K substitution where the maximal rate of absorption was reduced by 45%. These results imply that Na may not be required for substrate absorption under in vivo conditions where adequate circulation tends to maintain the proper intracellular ionic concentration. In the K experiment, K absorption and Na secretion were considerable and equal. Reduction in glucose $V_{\rm max}$ may therefore be due to the resulting intracellular ionic changes.

RESPONSES OF ATRIAL RATE TO VENTRICULAR RATE IN THE CONSCIOUS DOG WITH COMPLETE A-V BLOCK(AVB). W.C. Farr, J.L. Robinson, G.Grupp, & R.L. Barnard. Dept. Physiology and Internal Medicine, Col. Med., Univ. Cincinnati, Cincinnati, Ohio, U.S.A. Chronic complete AVB, induced by formalin, resulted in an atrial rate (AR) of 100

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Chronic complete AVB, induced by formalin, resulted in an atrial rate (AR) of 100 bpm and a ventricular rate (VR) of 40 bpm. In the resting unanesthetized dog, transient ventricular pacing (VP) for 2-20 min at rates of 60-200 bpm, 4-14 days post-op, caused profound decreases of AR (AR=0-20 bpm) that was maintained for the duration of a pacing period. VP above 240 bpm does not cause the marked atrial slowing. In anesthetized AVB dogs, and unanesthetized dogs without AVB, VP never leads to marked atrial bradycardia or asystole. In unanesthetized AVB dogs, all effects of VP on AR are abolished totally by: 1) methscopolamine plus propranolol or 2) methscopolamine plus hexamethonium. The effect of VR on AR is also reduced by chronic pacing at a VR of 120 bpm for 7 or more days. To determine the mechanism, we determined the pressure threshold in the perfused carotid sinus, that causes systemic blood pressure effects, of anesthetized normal and AVB dogs. We found the threshold to be 80 mm Hg in the normals and 25 mm Hg in the chronic AVB dogs. Conclusions: the hemodynamic consequences of chronic AVB may increase the sensitivity of the baroreceptor reflexes to the blood pressure changes induced by VP resulting in marked reflex slowing of AR. These effects are reduced if the slow VR is prevented by chronic VP at fast rates. (Supported in part by the American Heart Association, Southwestern Ohio Chapter, and U.S.P.H.S. HE-06307)

PRESSOR PEPTIDES FROM KIDNEY CORTEX, J. C. Fasciolo; N. Risler. Dept. of Physiology, Univ. Nacional de Cuyo, Mendoza, Argentina.

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Purified alcoholic extracts from hog kidney cortex show pressor effect when injected intravenously in the anesthetized rat. Purest extracts so far prepared display pressor responses in amounts as low as 0.1 microgram. Pressor activity was also recovered from dog and rat kidneys.

Highly purified extracts passed through a G 15 Sephadex column show three pressor peaks. On the same column peak I precede the peaks of Angiotensin I or II or Vasopressin. Peak II is in the zone of elution of these three peptides and peak III appears latter. The pressor activity found in these three peaks is completely destroyed by pepsin, trypsin, chymotrypsin and carboxypeptidase B.

502 STUDIES ON THE MECHANISM OF ACTIVE AMINO ACID TRANSPORT BY THE SMALL INTESTINE.

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The brush border or microvillous membrane of the mucosal cell, which is responsible for the active transport of certain amino acids by the small intestine, was employed to study the initial Na[†] dependent step in the mechanism of active intestinal amino acid transport. Isolated intact brush borders, containing a Na[†] concentration of 270 μ M, preferentially bound actively transported ^{14}C -labelled amino acids. Competitive inhibition experiments indicated that the binding sites for actively transported L-alanine, L-proline, and L-histidine are not the same, but may be in close proximity to each other. Osmotically disrupted brush borders were separated into 5 fractions by density gradient centrifugation on 10, 20, 30, 35, and $^{40}\text{\%}$ Ficoll. Actively transported ^{14}C -labelled amino acids were preferentially bound to the top fraction I. This fraction contained many filaments and had a relatively low Na[†] concentration (10 μ M). Preferential binding of ^{14}C -L-histidine to fraction I was dependent on the Na[†] concentration in the incubation medium. Binding was completely inhibited when NH₄ and Li were substituted for Na[†]. The replacement of Na[†] by K[†] produced an 81% inhibition of preferential binding. These results support the hypothesis that preferential binding of actively transported amino acids to a component within the brush border membrane is related to the initial step in the mechanism of active amino acid transport by the small intestine. Supported by N.I.H. AM07998.

PURIFICATION AND PROPERTIES OF A GONADOTROPIN RELEASING FACTOR. C.P.

Fawcett and S.M. McCann. Univ. of Tex. Sw. Med. Sch., Dept. of Physiology,
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Radioimmunoassay of LH and FSH has permitted significant advances towards the isolation of the hypothalamic factors controlling their release. A nine-stage purification procedure, including ultrafiltration, gel-filtration, adsorption chromatography, low-voltage thin layer electrophoresis and thin layer chromatography has yielded a preparation which causes a 2.5 fold increase in LH release in vitro, at a dose of 2 ng peptide per pituitary. This preparation also causes FSH release in vitro. Sufficient material was not available to obtain satisfactory evidence of homogeneity. Qualitative analysis after hydrolysis revealed the presence of 6-8 amino acids and indicated that only 0.05 $\mu\rm M$ peptide had survived from 100,000 fragments of sheep tissue. Available evidence indicates a maximum molecular weight of 1,000, some possibility of a single positive charge per molecule and considerable hydrophobic character, for LRF. Further analytical work is now being carried out with the aid of a new ultrasensitive method of amino acid analysis.

BIOCHEMICAL BASIS FOR O2 SENSITIVITY OF THE DUCTUS ARTERIOSUS. F.S.Fay, Physiol. Dept., Univ. Mass. Med. Sch., Worcester, Mass., USA

Studies were undertaken to elucidate the mechanism underlying the marked reversible contraction of the ductus arteriosus in response to increased oxygen pressure (P_{02}) . Ducts from newborn guinea pigs were mounted so that their lumen and outer surface could be independently exposed to controlled P_{02} during isometric measurements of muscle tension. Halfmaximal force was developed when both surfaces were exposed to 70 mm ${\rm Hg}$, ${\rm P}_{02}$. Inhibitors of oxidative phosphorylation selectively inhibited the contractile response to 0°_2 with little effect on the contractile response to acetylcholine. Oxygen consumption of ducts was measured as a function of P_{0_2} and was shown to be limited by intracellular 0_2 availability precisely over the range where muscle tension was dependent on P_{02} . Spectrophotometry on the intact tissue yielded oxidized/reduced difference spectra characteristic of a typical mammalian cytochrome chain. Following a rapid increase in P_{02} , cytochrome a_3 became oxidized, as measured spectrophotometrically, several seconds (2-40 sec.) before any detectable increase in muscle force. Further evidence supporting a primary interaction between $\boldsymbol{\theta}_2$ and cytochrome a_3 was provided by studies with CO, which produced an inhibition of the 0_2 response that was reversed by light. A model is proposed whereby contraction of ductal smooth muscle in response to 0_2 occurs because of an increase in the rate of synthesis of high-energy phosphate that results from increased availability of $^{0}2$ to the respiratory chain.

OCCURRENCE OF HUMAN SEMINAL PLASMA ANTIGENS IN THE TISSUES OF WOMEN. Sally De Fazio and Melvin M. Ketchel. Dept. of Physiology, Tufts University School of Medicine, Boston, Massachusetts, U.S.A.

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Seminal plasma proteins have been considered to include (1)blood plasma proteins and (2)"seminal plasma specific" proteins. Since female animals may be immunized via their reproductive tracts, they would be expected to become sensitized to seminal plasma specific antigens as a result of their sexual activity. In order to determine if "seminal plasma specific" proteins actually exist, we tested rabbit anti-human seminal plasma antiserum against extracts of a variety of human female tissues and fluids. A total of 23 antigens appeared in the seminal plasma of 8 donors, though no more than 21 antigens were found in the seminal plasma of any individual. Of the 23 antigens, seven were found in blood serum, and ten more were found in one or more of the following tissues and fluids: kidney, cervix, cervical mucus, endometrium, Fallopian tube, gastric fluid, milk, nasal secretion, ovary, saliva, urine and vaginal mucosa. While six seminal plasma antigens are still unaccounted for, the present data indicate that, at least for 17 of the 23 antigens found in seminal plasma, sensitization does not occur in women because the antigens are recognized as "self".

EFFECT OF ACOUSTIC STIMULATION ON THE SYNAPTIC VESICLES OF NERVE FIBERS AND TER - MINALS IN THE CEREBRAL CORTEX OF THE CAT. O. Fehér, F. Joó, N. Halász. Inst. of Animal Physiology, Lab. of Electron Microscopy, University of Sciences Szeged, Hungary.

Evoked potentials were elicited in the acoustic cortex of cats by applying unilateral rhytmic click stimulation of 20 cps frequency and 45 min. duration. The evoked potentials showed a marked decrease over the whole period of stimulation. Samples of the IV-V cortical layers were dissected from the site of recording and taken under routine electron microscopic examination. Densities of synaptic vesicles in the axon profiles of the stimulated and unstimulated sides were compared. The influence of anaesthesia could also be examined.

The vesicle densities were higher in awake and anaesthetized cortex by pentobarbital than in chloralose anaesthesia. Upon stimulation the changes of densities in axons of different diameter displayed a complex pattern. In axons of 0,1-0,3 μ^2 diameter the stimulation seemed to heighten the vesicle density, while in some categories of axons of 0,2-0,3 μ^2 diameter, a marked fall of the density was observed. Significant differences appeared in the vesicle density distribution between transient and synapsing axons.

CONTROL OF FOOD INTAKE IN INSECTS. D. Feir and E. McClain. Dept. of Biol. St. Louis Univ., St. Louis, Mo., U.S.A.

Two mechanisms of feeding control in Oncopeltus fasciatus were examined: (1) Volume of liquid in the hemolymph. The insects were injected with one of the following solutions: 1 or 4 ul water, or 1 or 4 ul of either 0.001M or 0.5M glutamine, histidine, alanine, or glycine. Then the insects were fed on a solution of 0.1M of one of the amino acids, and the imbibed volume was recorded. The larger the injected volume, the smaller was the volume imbibed by the bug. (2) Level of metabolite (amino acids) in the hemolymph. Either alanine, glycine, glutamine, or histidine was fed to or injected into the bugs. The number of subsequent feeding attempts and the duration of each feeding attempt on milkweed seeds was determined using time lapse photography. The imbibing of glutamine or histidine increased the number of feeding attempts. The first appearance of the amino acid in the hemolymph after ingestion, and the length of time it stayed there after ingestion or injection were ascertained using radioactive amino acids. The quantity of individual amino acids present in the hemolymph after feeding was monitored with a gas liquid chromatograph.

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REMOVASCULAR HYPERTENSION IN THE DOG. Agnes Fekete. Inst. of Physiology, University Medical School, Budapest, Hungary. 508

Following complete ligature of one renal artery with undisturbed contralateral kidney hypertension develops. The hypertensive state produced permits the continuous observation of the functional parameters of the un-

permits the continuous observation of the functional parameters of the undisturbed kidney. The hypertensive dogs have been observed for as long as 1-2 years. It was found that:

/l/removal of the ischaemic kidney das not lead to normalization of arterial pressure; /2/there is a gradual decline in the function of the undisturbed kidney: a drop in filtration rate, asthemuria with compensatory polyuria manifest; /3/a smaller fraction of ingested water, but a greater fraction of injected salt loads are excreted during the 150 min observation period as compared to the normotensive state; /4/plasma and blood volumes and extracellular space are reduced; /5/remin activity in the venous blood of the undisturbed kidney is enhanced even months after the removal of the ligated kidney; /6/small arteries of the undisturbed kidney are affected by degenerative changes /myoelastofibrosis/. The hypertension following unilateral ligation of the renal artery can be considered as a model of human renovascular hypertension.

. CHLORPROMAZINE-COCAINE ANTAGONISM : ITS RELATION TO CHANGES OF DOPAMINE 509 (DA) METABOLISM IN THE BRAIN. M.Fekete and J.Borsy. Res.Inst.for Pharmaceutical Chemistry, Budapest, Hungary.

Chlorpromazine or cocaine alone retarded the utilization of dopamine in the caudate nuclei of mice after the inhibition of catecholamine synthesis by a-methyltyrosine. Administration of the mentioned drugs together elicited a rapid decrease of the dopamine concentration in the striatum of mice given a-methyltyrosine. Cocaine augmented the increase striatum of mice given α -methyltyrosine. Cocaine augmented the increase in homovanillic acid concentration of the caudate nuclei of rats induced by chlorpromazine. In cocaine treated mice the increased formation of dopamine elicited by chlorpromazine was less pronounced as measured after a single intravenous injection of $^{14}\text{C-tyrosine}$. The results may be explained by the effect of cocaine inhibiting the reuptake of dopamine on the basis of a two-(or multi-)compartmental storage system of the transmitter.

CORRELATIONS BETWEEN EXPLORATORY BEHAVIOUR, HIPPOCAMPAL THETA ACTI-510 VITY AND PITUITARY-ADRENAL FUNCTION. T. Fekete, E. Endroczi and K. Lissák Department of Physiology, University Medical School, Pécs, Hungary.

Daily rhythm of plasma corticosterone level was correlated to the intensity of exploratory activity and duration of hippocampal theta rhythm in the experimental situation in adult male rats. An inverse correlation of plasma corticosterone concentration to the intensity of exploration was found when testing of exploratory behaviour was performed at the morning, afternoon and midnight hours. Duration of hippocampal theta activity was closely correlated to the intensity of exploration, and showed an inverse relation to the daily fluctuation of plasma corticosterone level. Corticosterone administration suppressed both exploratory scores and appearance of hippocampal theta activity during testing in a 12-cell experimental cage. It was concluded that hippocampal activity plays a basic role in corticosterone adjusted changes of behaviour, on the one hand, and fluctuation of exploratory participations and death activity by light and death periods to mediated ation of exploratory activity by light and dark periods is mediated through pituitary-adrenal function.

DOES LEUCOCYTE PYROGEN ENTER THE ANTERIOR HYPOTHALAMUS VIA THE CEREBROSPINAL FLUID? W.S. Feldberg, W.L. Veale & K.E. Cooper, The Lab. of Neuropharm., The Natl. Inst. for Med. Res., London, England, and Div. of Med. Physiol., Univ. of Calgary, Calgary, Canada.

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Leucocyte pyrogen induces a fever in the rabbit when it is injected into the anterior hypothalamic-preoptic area (AH/POA) in µl volumes. The amount of leucocyte pyrogen needed to elicit a febrile response when injected into this area is more than 100 times less than that needed to induce fever by intravenous (iv) injection of the same substance. Further, the interval between the injection of leucocyte pyrogen into the AH/POA and the resulting temperature increase is 3-10 min whereas that following iv injection is 15-20 min. Experiments were carried out to test the hypothesis that following the iv injection of leucocyte pyrogen it enters the fluid of the ventricular cavities of the brain and then penetrates the ependymal wall into the AH/POA. The cerebral ventricles of unanaesthetized rabbits were perfused from a lateral ventricle to the cisterna magna with artificial cerebrospinal fluid (CSF) at a rate of 1.3 ml per 10 min. During this time leucocyte pyrogen was administered iv but the onset, magnitude or duration of the febrile response was not different from that in non-perfused animals. In addition, perfusion of the ventricles with a 1-20 dilution of the same leucocyte pyrogen for 10-20 min, preceeded and followed by perfusion with artificial CSF was not as effective in eliciting an increase in temperature as was iv injection. Dye perfused in a similar manner stained the entire wall of the 3rd cerebral ventricle. These results suggest that leucocyte pyrogen given iv enters the AH/POA directly from the blood stream rather than via the CSF.

LIIOLYTIC ACTIVITIES IN THE ABOLWSUM OG THE FRE-RUMINANT CALVES.
L.Feliński, Gr. Kaczmarek. Inst. of Applied Biology, Zootechnical Faculty, College of Agriculture, Szczecin, Foland.

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Three calves 18,9 and 12 days old were used in this study. Each animal mas fitted with a re-entrant cannula to the duodenum behind pylorus. In this form of cannulation the duodenum was transected. The calves were fed with whole poudered milk, ad lib. Digesta were collected for a period of 7 h and the flow-rate /ml/h/ was recorded. The lipids removed of digesta and analysed by the Bligh and Dyer method. The composition of fatty ecids was determined by gas-liquid chromatography. In the milk used there was a 1 mass from the digesta passing from the abomasum to duodenum - from 9 to 32 mass from the gatest extent of TG hydrolysis in abomasum occurred during 5th,6th and 7th h after feeding. After the histamine injection /0.0lmg/kg/ a decrease of TG hydrolysis was observed. When insuline was injected /0.4 i.u./kg / an increase of TG hydrolysis was recorded.

In the period of 7 h from the abomasum to duodenum is entering from 19 to 49 m lipids consumed. On the lipidless diet, there was practically no FFA and other lipids in the digesta entering the duodenum.

METABOLISM OF ESTROGENS BY RAT PROSTATE AND SEMINAL VESICLE. Montserrat dem. Fencl, N. Bashirelahi, and C.A. Villee. Dep. of Biol. Chem., Harvard Medical School, and Boston Hospital for Women, Boston, Mass., U.S.A.

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In the rat, the prostate and the seminal vesicles, both target tissues for androgens, respond differently to estrogens: the regression after castration is augmented by administration of estradiol-178 (E2) in the prostate and not in the seminal vesicle (Fujii & Villee, Endocrinology 83:1140, 1968). We have found that 2 hours after injection of $^3\text{H-E2}$ into rats more estrone (E1) was isolated from the prostates than from the seminal vesicles. This was true in both normal and castrated rats. In vitro incubations with $^3\text{H-E2}$ or $^3\text{H-E1}$ showed that prostates of normal and castrated rats metabolized about 80 % and 50 % of E2 to E1, respectively; when $^3\text{H-E1}$ was the substrate, 80-90 % of the radioactivity remained unconverted. Seminal vesicles of normal and castrated rats incubated under identical conditions left 90 % of both of the substrates unconverted. These results show that (1) both the prostate and the seminal vesicles of rats can metabolize estrogens; (2) the prostate has a greater capability than the seminal vesicles to convert E2 to E1; (3) in the prostate, the interconversion of E2 and E1 is preferentially in the direction of oxidation.

EFFECT OF CERVICAL SYMPATHECTOMY ON THE FORMATION OF THE "MINIATURE NEURO-HYP-PHYSIS" AND ON THE WATER HOUSEHOLD AFTER HYPOPHYSIAL STALK SECTION IN RAT. K.Fendler, I. Vermes, A. Stark and K. Lissák. Dept. of Physiology, Univ. Medical School, Pécs, Hungary.

It has been reported that the regeneration stump developed after hypophysial stalk section can be inhibited with oxytocin treatment in the rat. It was also found in our earlier experiments, that cervical sympathectomy inhibited the hypothalamic magnocellular naurosecretory system. In present experiments we have shown that the cervical sympathectomy moderated the stalk section induced polyuria and polydipsia in rat. Two weeks after operation the cervical sympathectomy prevented the accumulation of neurosecretory material in the proximal stump of the hypophysial stalk. There was no correlation between the regeneration of the anterior lobe and formation of the "miniature neurohypophysis". The ADH content of the "miniature neurohypophysis was in agreement with the histological picture.

PARTIAL MOLAL VOLUMES OF OXYGEN, CARBON MONOXIDE AND CARBON DIOXIDE IN BLOOD. W.O.Fenn. Department of Physiology, School of Medicine and Dentistry, University of Rochester, Rochester, New York, USA.

Before and after equilibrating blood with 0_2 , CO or CO₂ measurements were made either of the weight of a constant volume (pycnometer) or the volume of a constant weight of blood or cell suspension. In this way it was found that oxygen added to blood apparently decreases the volume of the Hb molecule, or it goes into a void in the molecule where it occupies no additional volume. The average partial molal volume of oxygen in HbO₂ in 116 experiments was 0.4 \pm 3.5 ml/mole, while the value for oxygen in physical solution in water is 31 ml/mole. Carbon monoxide behaves much like oxygen, although the average value in 29 experiments by the volumeter and the pycnometer methods was 7.7 \pm 3.1 ml/mole. With carbon dioxide the partial molal volumes in water, dilute NaOH, plasma, and blood were found to be 33, 26.8, 19.6, and 12.9 respectively. These differences probably depend chiefly on the number of new ions produced by combination with CO₂ or binding as carbamino compound.

DIFFERENCE BETWEEN INOTROPIC AND CHRONOTROPIC β-ADRENOCEPTORS. T. Fenyvesi and P. Hadhazy. II. Medical Department and Department of Pharmacology, Semmelweis University Medical School, Budapest.

It has been suggested that there is no difference between cardiac eta-adrenoceptors responsible for the inotropic effects of sympathomimetic amines on one hand and for

their chronotropic effects on the other.

We re-investigated the problem on 24 dog heart-lung preparations. The cardiac output, left ventricular and right atrial pressures, the heart rate, the first derivatives of the aortic flow and pressure and of the left ventricular pressure were continuously monitored. The effects of increasing doses of three β -adrenoceptor blocking agents (propranolol, practolol and LB46) were estimated by the shift of the isoprenaline dose-response curves. 640 μg propranolol caused a 40.5-fold shift in chronotropic and a 16.8-fold shift in inotropic dose-response curves. 1280 μg practolol caused a 54.4 and 12.2-fold shift, 40 μg LB46 a 63.4 and a 15.9-fold shift respectively. As a result of this preferential blockade of the chronotropic effect, an isoprenaline-induced increase in cardiac output becomes dependent on increased stroke volume, whilst before β -adrenoceptor blockade it is dependent on increased heart rate.

We concluded that in the heart-lung preparation of the dog, β -adrenoceptor blocking agents cause a higher degree of blockade in the chronotropic than in the inotropic response to isoprenaline. This suggests a difference between the receptors involved.

SIMULTANEOUS RECORDINGS FROM MULTIPLE SINGLE UNITS IN CAT VISUAL CORTEX. R.D. Fernald & R. Chase. Max Planck Inst. of Psych., Munich 23, W. Germany.

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Electrical recordings in the central nervous system have produced descriptions of functional properties of single neural elements, but such measurements have not clarified the manner in which aggregates of neurons process information. For example, single cell recordings in cat visual cortex have revealed a functional organization whereby cells which share certain preferred stimulus features seem to be arranged in columns. However, the manner of synaptic connectivity within such a column, or between columns, has not been determined. The present study was designed to investigate this question with physiological techniques. Action potentials from groups of two or three discriminable neurons in cat visual cortex (17) were recorded by conventional techniques with two independently manipulated microelectrodes. Receptive field characteristics and ocular dominance for each unit were determined by exploring the visual field with small spots and slits of light. Spontaneous activity and stimulated responses were recorded concurrently for all units and the data analyzed statistically. We identified excitatory and inhibitory connections between cells as well as common synaptic inputs with the "joint peristimulus time histogram." This information was related to the previously determined functional characteristics of each cell and to the physical location of the cells as determined by histological examination of small electrolytic lesions made at the recording site.

SEXUAL DIFFERENCE IN THE EFFECT OF ANGIOTENSIN ON WATER INTAKE IN NEPHRECTOMIZED RATS. L.A.Fernandez, R.H.Mejia and V.G.Foglia. Inst. of Physiology, Sch. of Med., Univ. of Buenos Aires, Buenos Aires, ARGENTINA

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The dipsogenic action of renin and angiotensin has been demonstrated. Angiotensin was given at the doses of 20 ug and 40 ug each hour for three hours. Difference in water intake after angiotensin administration was statistically significant in females to a greater extent than in males. The post-pubertal castration either in males or females did not modify this response, nor did gonadectomy of females at birth. Nevertheless, in males castrated at birth, in responce to angiotensin administration water intake increased to the same level as that of the females.

This action is independent of the sexual hormones; however, it seems to be related with the inductive effect of the sexual hormones on certain areas of the central nervous system during the first days of life.

EFFECT OF HYPOPHYSECTOMY ON THE DISTRIBUTION OF WATER IN GONADS AND SEXUAL ACCESSORY ORGANS IN THE RAT. E.L. Fernandez-Collazo, L.A. Fernandez, R.H.Mejia, A.Rosenkrantz and R.E.Mancini. Ctr. of Studies on Reproduction and Inst. of Physiology, Sch. of Medicine, Univ. of Buenos Aires, Buenos Aires, ARGENTINA.

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Total water, determined by dessication, and extracellular space as a sodium space, were measured in testis, epididymis, seminal vesicle and submaxilary gland from normal and hypophysectomized Wistar rats. Two months after hypophysectomy, total water did not show any significant difference in these organs. Sodium space increased two and one half fold in testis of hypophysectomized animals. This increment was less evident in epididymis and seminal vesicle. No changes were found in submaxilary gland. Intracellular water, calculated as a difference between total water and extracellular water, showed a significant decrease in testis, epididymis and seminal vesicle.

Hypophysectomy produces changes in the distribution of water in gonads and secondary sexual organs. This redistribution of water may be due to a lack of gonadotrophins, principally LH, and/or the secondary diminution of androgens release.

CORRELATIONS BETWEEN PRECENTRAL CELLS AND ARM MUSCLES DURING DIFFERENT OPERANTLY REIN-FORCED RESPONSE PATTERNS. E.E.Fetz and D.V.Finocchio. Reg. Primate Res. Ctr. and Depts. of Physiol. & Biophys. and Neurol. Surg., Univ. of Washington, Seattle, Wash. 98105 (USA).

In awake monkeys we recorded activity of single precentral cells, 4 contralateral arm muscles (a flexor and extensor of wrist and elbow), and position of the elbow under several behavioral conditions. (1) We tested each cell's response to passive joint movements and cutaneous receptive fields while rewarding the monkey for sitting quietly; most cells responded to passive joint movements without any recorded EMC activity. (2) With the arm held semiprone in a cast hinged at the elbow, we reinforced active elbow movements; many cells responded during some phase of these movements. With the cast immobilized, we reinforced patterns of muscle and cell activity. (3) Reinforcing isometric contraction of each of the 4 muscles in isolation produced bursts of EMC activity predominantly or exclusively in the appropriate muscle; usually cell activity was most strongly correlated with one or more specific muscles. (4) Reinforcing bursts of cortical cell activity produced correlated bursts of EMG activity in several arm muscles, including those correlated with the cell in (3). (5) Reinforcing bursts of cell activity with simultaneous suppression of EMG activity produced suppression of all EMG activity. Thus, correlations between a precentral cell and specific arm muscles may consistently appear in a variety of behavioral conditions but also may be dissociated by operant reinforcement of cell activity with simultaneous suppression of EMG activity. (Supported by NIH grant FR00166, FHS 5T1 NB 5082-13 and NIMH 35745-02.)

521 SUPPRESSION OF EXPERIMENTAL RENAL HYPERTENSION BY HYPOTHALAMIC LESIONS IN RATS. F.P. Field and K.J. Kant, Dept. of Physiol. State Univ. of N.Y. at Buffalo, Buffalo, N.Y., U.S.A.

Previous investigators have shown that direct interference with thyroid gland activity prevents development of experimental renal hypertension in rats and also reduces the severity of existing experimental renal hypertension. It is possible that lesions placed in the hypothalamus could significantly disrupt the feedback control system for the thyroid gland and result in a similar suppression of experimental renal hypertension. To test this possibility, renal hypertension was induced in rats through encapsulation of both kidneys with latex envelopes either prior to or following the production of electrolytic lesions placed bilaterally in the hypothalamus. Changes in systolic blood pressure were monitored with a tail cuff method, and hypertension was defined as a systolic blood pressure greater than 150 mm Hg. The bilateral lesions were placed in the posterior portions of the paraventricular nucleus. The results of these studies demonstrated that the development of renal hypertension could be prevented when renal encapsulation was preceded by formation of lesions in the hypothalamus. Furthermore, similar lesions placed in rats with established experimental renal hypertension resulted in a significant decrease in systolic blood pressure. Several thyroid function tests were performed on the rats in these studies, and the results showed reduced thyroid activity in the lesioned rats when compared to the controls. Therefore, it is suggested that suppression of the development of experimental renal hypertension and reduction in severity of established renal hypertension in the lesioned rats are results of reduced thyroid gland activity.

522 INVESTIGATIONS CONCERNING THE VALUE OF RHEGENCEPHALOGRAPHIC METHOD IN ASSESSING BRAIN CIRCULATORY MODIFICATIONS IN YOUNG PEOPLE. V.Filescu, I.Pintilie, C.Cristescu, Aeronautical Medical Centre, Bucherest, Romania.

Four groups of young pilots (aged between 18-30 years) were studied in order to follow up the evolution of some haemodynamic parameters (heart frequency, systolic and diastolic blood pressure) and rhecencephalographic parameters (sphygmic celerity and velocity, celerity index, Kunert index, relative pulse-volume, wave amplitude) under the influence of Valsalva mancever and of posture variations, of anti-G costume, of effort and of 02 loo% breath normober on the ground and at 5,500 m altitude in barochamber, of 02 loo% breath hyperbar (at 300 m H20) and of some vasc-active substances (hydergine, amylnitrite). The modifications of brain vascular tonus and of brain blood flow were accompanied by important modifications of rhecencephalographic parameters. The authors discuss for each separate group the mathematical and biological significance of REG and haemodynamic modifications which have been found out.

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MECHANISM OF ACTION OF GLUCOCORTICOIDS: EFFECT ON THE REDUCING POWER OF NAD SYSTEM. Anna Fiorentini, Maria L. Fabiani, Inst. of Physiology Univ. of Milan, Milan, Italy. The early increase in blood glucose induced by hydrocortisone (HC) is known to be independent of enzyme synthesis, but the mechanism of this effect is unknown. The present investigation shows that HC administration in non-anaesthetized rats, chronically cannulated, induces a sharp increase of the reducing power of NAD system in plasma, which precedes the blood glucose rise. The early increase in NADH/NAD ratio disappears as blood glucose increases, this effect appears to be due to the release of insulin. Actinomycin D, which prevents the synthesis of enzymes does not affect the increase of NADH/NAD due to HC. The rise in plasma amino-nitrogen and F.F.A.lags behind the rise in NADH and blood sugar: the increased NADH/NAD ratio cannot be due therefore to enhanced catabolism of lipids and proteins. The higher utilization of fructose than glucose after HC injection may be interpreted as a decrease of NADH. These results indicate that HC may regulate carbohydrate metabolism by directly affecting the level of red-ox of the NAD in cytoplasmas. The rise of the reduced form of NAD will impair glucose utilization and stimulate its synthesis in the tissues, owing to the involvement of this coenzyme in a reversible reaction of glucose metabolism. An adaptive synthesis of enzymes involved in gluconeogenesis may follow.

THE SIGNIFICANCE OF CONVOLUTION INTEGRAL FOR THE PHYSICAL AND NEURONAL TRANSFORMATION OF THE OPTICAL IMAGE IN THE EYE OF VERTEBRATES. B.Fischer and H.U.May. Neurologische Universitätsklinik mit Abteilung für Neurophysiologie, Freiburg i.Br., Germany.

The physical transformation of an optical image is described by the convolution of an input function I(r,t) and a transfer function T(r,t): \(\int T(r-r', t-t') \cdot I(r',t') \cdot dr'dt'. \) Spatial and temporal summation of retinal cells and their related thresholds may be calculated by integrals of the above form. T represents the sensitivity of a single neuron. This leads to the concept of 'neuronal images', formed by cell populations and their overlapping receptive fields. Determination of an appropriate transfer function for each system is attempted. Gaussian functions are useful for applications to two-dimensional spatial patterns in vision, whereas exponential functions are more convenient for time dependence. Luminance distributions of light patterns at the retina were calculated and presented graphically as the actual input to the receptor cells. The use of Fourier transformation allows for a uniform mathematical description of the physical and neuronal image transformation, which takes into account optical blurring in the eye. The convolution integral constitutes the basis of a more general and non linear theory of the visual information processing.

EFFECT OF VENTRICULAR MUSCLE MASS UPON MAXIMAL FORCE DEVELOPMENT. Vincent J. Fisher and Frederic Kavaler. Dept. of Physiology, Downstate Medical Center, State Univ. of N.Y. and Cardiology Section-Cardiopulmonary Laboratory, New York Veterans Admin. Hosp., USA

A comparison was made between maximal force developed by whole canine left ventricles and by single, coronary perfused right ventricular papillary muscles remaining in situ. The intact ventricles were studied by the isovolumic technique at the peaks of their pressure-volume curves. Chamber and wall dimensions were measured radiographically and circumferential stress was calculated. The papillary muscles were stretched to optimal length by a specially designed isometric, in situ force gauge. Maximal contraction was produced by paired pulse stimulation of 27-45 paired beats/min at 27°C . A linear relationship was found between papillary muscle thickness and maximal developed stress. The 16 muscles of < 10.1 mm² cross sectional area developed a force of 7.96 ± 1.69 g/mm², while the 30 muscles of > 10.0 mm² developed 5.32 ± 1.49 g/mm² (P<.001). The maximal circumferential stress developed by the ventricles $(5.80 \pm 0.93$ g/mm²) was not significantly different from that developed by the larger papillary muscles but was significantly less than the force of the smaller muscles (P<.01). Measured sarcomere lengths for both preparations showed a dispersion about optimal length but not of a magnitude to account for the difference in force development. There may be more fiber slippage when large muscle masses contract and hence a less isometric state. (Supported by New York Heart Assoc. and United States Veterans Admin.)

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526 CORRELATION OF TIDAL VOLUME AND PHRENIC NERVE ACTIVITY DURING HYPERCAPNIA AND HYPOXIA. Robert S. Fitzgerald. The Johns Hopkins University, Baltimore, Maryland 21205.

The response to respiratory stimuli is most frequently measured in terms of the total ventilatory response (V_T , f, V_E or V_R). The purpose of this study was to differentiate the contribution of the muscular elements which generate the total response. In five anesthetized cats one phrenic nerve was transected and placed on platinum electrodes. The activity was rectified and integrated. After a control period the cat was given either an 8% CO₂ in air or an 8-10% O₂ mixture to breath for 20-30 breaths until a relatively constant V_T appeared. Phrenic nerve activity/time (PE) was correlated with total volume (V_T) for each breath; PE was also correlated with V_T . The linear correlation coefficient (r) for the "on-hypercapnia" response was 0.907; for the "on-hypoxia" response it was 0.798. The slope of the "on-hypercapnia" response (PE, V_T) was 1.5-2.0 times the slope for the "on-hypoxia" response. In the correlation of PE, V_T for the "on-hypercapnia" response was 0.873 while that for the "on-hypoxia" response was 0.787. Again the slope of the "on-hypercapnia" response was 1.5-2.0 times the slope for the "on-hypoxia" response. If one adds CO₂ to the hypoxic mixture during hyperventilation so as to keep the FECO₂ constant, the slopes more closely approximate the hypercapnic response. If one accepts that phrenic nerve activity represents diaghragmatic activity, these results suggest that the diaphragm is more active in generating the respiratory response in hypoxia than to hypercapnia. (Supported in part by U.S.P.H.S. Grant HE 10342.)

527 EFFECTS OF PROLONGED EXERCISE ON VENTILATION AND ARTERIAL BLOOD IN RUNNING DOGS. R. Flandrois, J.R. Lacour, H. Osman and J.P. Eclache. Laboratoire de Physiologie A, Faculté de Médecine, 69-Lyon, France.

Ventilation and arterial blood have been studied in dogs, running on a treadmill at various speed and slopes; \hat{v}_{o_2} was increased up to 6,5 times the resting value. Ambient conditions were 18°C, r.h. 55%, 746 torr.

Ventilation which was studied cycle by cycle, increased immediately at the onset of the exercise and decreased suddently at the end. Slow ventilatory changes followed fast changes, in particular, after a few minutes of exercise appeared progressively a thermal polypnea. However, the ventilatory pattern during prolonged exercise is such that the alveolar ventilation change was roughly proportional to the change of $\hat{\mathbf{vo}_2}$ and $\hat{\mathbf{voo}_2}$ and that the arterial blood $\hat{\mathbf{Po}_2}$, $\hat{\mathbf{Poo}_2}$ and pH varied little.

THE INFLUENCE OF WEAK ACIDS ON ION TRANSPORT IN THE GASTRIC MUCOSA.

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Acetate, propionate and L-lactate (10 mEq/l) stimulated hydrogen ion secretion in the isolated frog (Rana temporaria) gastric mucosa. By use of this stimulatory effect it was shown that these acids accumulate in the gastric mucosal cells when present in the undissociated form on the secretory side of the mucosa. The dissociated antions of the same acids did not accumulate. Undissociated D-lactate did not stimulate and undissociated acetylsalicylate inhibited the secretion.

From determinations of the impedance locus diagram and the resistance of the mucosa it was shown that undissociated acetate, propionate and acetylsalicylate increased the ion permeability of the mucosa in vitro. The concentrations of acid used were the same as those earlier shown to increase the mucosal permeability on instillation into the intact mammalian stomach. It is probable that the intracellular accumulation of undissociated weak acids is the mechanism underlying their permeability effects on the gastric mucosa.

A SUMMARY INDEX FOR THE RESPONSE OF THE LIVING ORGANISM TO THE ENVIRONMENT. R.J.Florov, Higher Forestry Inst., and Zh.V.Stojanov, Forest Res.Inst., Sofia, Bulgaria.

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The rate of the metabolic heat is closely linked with the energy and matter exchange between the organism and environment: by intensive exchange the metabolic heat increases and by less intensive it decreases. Consequently, the metabolic heat is an index for the status of the organism, an index for its response to the environment. Our investigations ascertained it is possible to determine the metabolic heat by means of the rising entropy in the living organism. The entropy was determined by means of heat exchange and water exchange. The metabolic heat, established by means of the rising entropy, nearly coincided with the metabolic heat, determined after the food taken by the organism. For example, the metabolic heat of Richmondena cardinalis, determined on the ground of the food taken, was 0,076 cal cm⁻²min⁻¹, and the heat computed by means of the rising entropy was 0,084 cal cm⁻²min⁻¹/cm⁻² is relative to the body surface area/. Therefore, the summary index proposed for the reaction of the organism to the environment receives a broad field of application.

A POSSIBLE ELECTROGENIC COMPONENT IN THE TRANSMEMBRANE POTENTIAL OF RAT LIVER CELLS. M.Folke. Inst. of Med. Physiology, Dept. A, Univ. of Copenhagen, Denm.

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The hepatic cell membrane potential (HCMP), studied in vivo, shows a remarkable sensitivity to asphyxia or clamping of the hepatic vessels: within 5 minutes the potential is decreased from a normal value of 50 mV (inside negative) to 25-30 mV. In order to elucidate factors affecting the HCMP under controlled conditions, rat livers were perfused at 37°C with Krebs buffer containing red cells, albumin, and glucose. The oxygen consumption was only about half the value estimated for intact rat liver, but tissue contents of water, Na, and K were well maintained. HCMPs were in the range 26-33 mV and did not diminish, when anoxia for 1 hr was induced by substituting nitrogen for oxygen in the gas mixture equilibrating the perfusate. - The differences in oxygen consumption and HCMP between in vivo and in vitro conditions suggest that the HCMP has two components, one of which (present in vivo but missing in isolated liver) is dependent on the metabolic activity of the organ, while the 'remaining' part of the potential seems rather unaffected by lack of oxygen. This interpretation fits with the possibility that an electrogenic pump, dependent on a normal oxygen consumption, is involved in the maintenance of the hepatic cell membrane potential in vivo.

EFFECTS OF REGIONAL HYPOTENSION ON DESIGN AND HAEMODYNAMICS OF THE RESISTANCE VESSELS IN NORMOTENSIVE AND SPONTANEOUSLY HYPERTENSIVE RATS. B.Folkow, M.Gurevich, M.Hallbäck, Y.Lundgren, L.Weiss. Dept. of Physiology, Univ. of Göteborg, Sweden.

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The altered resistance and vascular "reactivity" in hypertension is largely dependent on an adaptive structural change of the resistance vessels, markedly changing their haemodynamic characteristics, even at an unchanged smooth muscle activity (Folkow et al. 1970). – In young spontaneously hypertensive rats (SHR) and normotensive control rats (NCR) the aorta was ligated distally to the kidneys, reducing the hindquarter pressure 30-40 %. 6-16 weeks later these hindquarter preparations were isolated and perfused at constant flow in parallel with unligated NCR or SHR. They displayed marked decreases in flow resistance at maximal dilatation, in steepness of the doseresponse curve and maximal pressor response to pressor agents, but vascular smooth muscle sensitivity to such agents was largely unchanged. This indicates a rapid structural adaptation of the resistance vessels in the artificially hypotonic hindquarters of NCR and SHR in terms of reduced wall thickness and increased lumina, even during maximal dilatation. – Thus, any alteration of pressure appears to rapidly affect vascular design, largely explaining the considerably changed haemodynamics in hyper– and hypotension.

B.Folkow, M.Hallbäck, Y.Lundgren and L.Weiss. Acta physiol. scand. 1970. 80, 93-106.

LACK OF THRESHOLD FOR URATE EXCRETION BY THE HUMAN KIDNEY AT URICASE-LOWERED PLASMA LEVEL. C.Fontenaille, P.Pfluger, M.Jozefowicz, R.Royer, P.Guiheneuc, M.Boulangé. Univ. Hosp. Nancy and Nantes, and scientific Ctr., St.Denis, FRANCE.

(1) In man, the mechanisms of urate excretion are 'nt well known, particularly at low plasma levels. (2) Uricase was injected in ten normal men in order to attain urate plasma levels (P.ur.) as low as 0,5 mg/l, net reabsorption beeing calculated at various P.ur. by clearance methods. (3) As low as P.ur. might be, we did'nt observe any excretory threshold. Urate clearance (C.ur.) followed a biphasic curve and was higher at P.ur. below 10 mg/l than at normal levels. (4) Those findings may be interpreted by two hypothesis: (a) three components mechanism: at low P.ur., tubular secretion account for the excreted urate, and C.ur. decrease with the increasing P.ur. until reabsorption occurs; (b) an unidirectional transfer: one must assume that a minimal level of urate is necessary to the carrier-urate complex formation. Such a reabsorption threshold may occur if the carrier concentration is higher at the luminal than at the peritubular side, and if, the apparent equilibrium constant of the reaction is higher at this side. Modifications in physical solubility or ionization of urate may explain this later difference.

THE EFFECT OF CLOSED INTRARENALLY INFUSED HYPERTONIC UREA ON THE RENAL HEMODYNAMIC AND RENIN RELEASE IN DOG. I.Forgács and Katalin Gaál. Inst. of Physiology, Semmelweis Medical University, Budapest, Hungary.

The factors influencing the rate of renin release are still poorly defined. Experiments were performed on 20 mongrel dogs anesthetized with pentobarbital. Ten dogs were fed with a sodium-poor diet /hyponatraemic reninrich kidney group:"A"/, while 10 dogs were loaded with hypertonic saline /hypernatraemic renin-poor kidney group:"B"/ previously the experiment. Following the control periods 5.1±1.9 ml/min. 20 per cent urea was infused into the left renal artery for five minutes. In group "A" the renal blood flow, creatinine- and PAH extraction ratio decreased, the renal vascular resistance, the water- and sodium output, and the renin activity in the renal venous blood increased significantly. There were no changes in the group "B". Following the administration of 10.3±3.0 ml/min. of 20 per cent urea the same changes were found in group "B" as in group "A" after the lower urea infusion. These findings suggest that hypertonic urea infused into the artery of the renin-rich kidney stimulates renin release either by acting osmotically, or by increasing the distal tubular sodium load, and/or by altering some aspect of the renal circulation. To get the same effect in renin-poor kidney a higher amount of urea infusion is necessary.

534 IS THERE A COUPLING BETWEEN THE INTESTINAL ABSORPTION OF GLUCOSE AND SODIUM? H. Förster and I. Hoos. Institut für vegetative Physiologie, University of Frankfurt (Germany).

The absorption of glucose from the small intestine of rat perfused with sodium-containing or sodium-free solutions was investigated by three different methods: 1. in vivo; 2. in vitro, with the vascular circulation maintained and the liver included in the circulation; 3. in vitro, with the vascular circulation maintained and the liver excluded. The glucose concentration in the perfusion solution varied between 0 and 60 mM. Besides this 270 mM of xylitol or 150 mM of NaCl were added to obtain blood isosomotic conditions. Glucose absorption was almost unaffected by the absence of sodium from the intestinal lumen. Under in vitro conditions the absorption of glucose was reduced to 50 %, and the excretion of sodium (sodium free solutions) into the intestinal lumen increased by about 50%. Under in vivo conditions the excretion of sodium into the lumen of the small intestine was 0,5 mval/h, independent of the glucose concentration; though the absorption of glucose varied between 0 and 1,5 mmol/h. In in vitro investigations the elimination of sodium was 0,7 mval/h and the absorption of glucose varied between 0 and 0,8 mmol/h. In view of these results a direct coupling between the absorption of glucose and that of sodium seems unlikely.

GLYCOPROTEIN AND GLYCOLIPID ASSOCIATED WITH GASTRIC HC1 SECRETION.

Forte. Dept. of Physiology and Donner Laboratory, Univ. of Calif., Berkeley, Calif. 94720 Cytochemical and biochemical analyses for glycoproteins were carried out on intact bullfrog gastric mucosa and subcellular fractions therefrom. Using the HIO4-Ag methenamine staining method (Ag-stain) the Golgi apparatus, smooth tubular membrane system and

apical cell membrane of oxyntic cells were strongly reactive for sugar components. A technique was developed to denude gastric mucosa of surface mucous cells. The mi-

crosomal fraction (40,000xg) from oxyntic cell homogenates reacted with the Ag stain in a manner characteristic of the tubular membranes of intact cells, thus indicating the cellular origin of this fraction. Analysis of the microsomal fraction showed that it contained about 150 mg carbohydrate/gm protein. Approximately 30-40% of the carbohydrate was characterized as glycolipid--the remaining being glycoprotein. Pronase digestion of the glycoprotein produced a large molecular weight glycopeptide (60%) and two small glycopeptides (40%). The large glycopeptide (>10,000 mw) contained the following proportion of carbohydrates: hexose = 22, glucosamine = 20, fucose = 14 and sialic acid = 1. The smallest of the low molecular weight components contained only hexose while the other glycopeptide contained hexose, aminosugars and fucose in a 3:3:1 proportion. Cytochemical localization of the Ag-stain was consistent with an hypothesis whereby the tubular membranes of oxyntic cells are synthesized in the Golgi region and participate in gastric HCl secretion. isolated glycopeptide constituents are the likely components which give the positive cytochemical reaction. (Supported in part by USPHS)

STIMULATION OF RAT KIDNEY PLASMA MEMBRANE ADENYL CYCLASE BY VASOPRESSIN AND PARATHYROID HORMONE. Leonard R. Forte. Pharmacology Department, University of Missouri, School of Medicine, Columbia, Missouri, U.S.A. 65201.

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The mammalian kidney is a target tissue for vasopressin and parathyroid hormone. Both hormones activate renal adenyl cyclase in vitro and presumably in vivo. In vitro stimulation of renal adenyl cyclase has been studied in crude particulate fractions from rat kidney. However, the adenyl cyclase is considered to be specifically localized in the plasma membrane of cells. This study utilizes a purified plasma membrane preparation from rat membrane of cells. Inis study utilizes a purified plasma membrane preparation from rat kidney. The specific activity of the adenyl cyclase of rat kidney plasma membranes is higher than any other subcellular fraction tested (i.e. homogenate, nuclear, microsomal and cytoplasmic). The activity of cyclic 3', 5' AMP phosphodiesterase of the plasma membrane preparation is about one-third the activity found in the soluble cytoplasmic fraction of rat kidney. Both vasopressin and parathyroid hormones enhance the basal adenyl cyclase activity three to four fold. In contrast, sodium fluoride stimulates the rat kidney plasma membrane adenyl cyclase more than twenty fold. It is concluded that vasopressin and parathyroid hormones may interact with specific renal plasma membrane vasopressin and parathyroid hormones may interact with specific renal plasma membrane receptors which are associated with the plasma membrane adenyl cyclase system. Supported by U.S. Public Health Service Grant AM-14787.

ALTERATION OF IONIC MEMBRANE CURRENTS OF RANVIER NODES BY MONO-CHROMATIC UV-RADIATION. J.M. Fox and R. Stämpfli. I. Inst. of Physiology, Univ. d. Saarlandes, 665 Homburg-Saar, F. R. Germany.

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Isolated Ranvier nodes of the sciatic nerve of rana esculenta were irradiated by monochromatic u.v. radiation (280 nm) under voltage clamp and current clamp conditions. The most abvious effect was found to be an expontential decrease of the maximum sodium inward current with dose. An e-fold reduction is produced by a u.v. dose of about 13 mW/mm². The rate constant of decrease is proportional to the dose rate within a range of about 80 to 320 erg/mm² sec. This suggests that the probability of blocking a pathway for sodium by u.v. radiation is proportional to the number of remaining functional pathways. The most striking result is, that the potassium current is not affected significantly by the same irradiation. Accordingly current clamp experiments reveal high sensitivity of the rate of rise of the action potential to u.v. irradiation of this wavelenght. An "initial enhancement of activity" as described by others was never observed. During irradiation to a loss of excitability no marked changes of other membrane properties such as leak- and potassium-conductance can be observed. The equilibrium potential for sodium remains constant, the resting potential is not lowered by more than $10\,\%$ (including run down of the fibre). Measurements with other wavelenghts are in progress and will be reported.

538 EFFECT OF PENTOBARBITAL ON THE REVERSAL OF SPLANCHNIC AFFERENT BLOOD PRES-SURE RESPONSES. Z. Franc, J. Siegelová. Dept. of Physiology, Med. Faculty, University J.E. Purkyne, Brno, CSSR.

The blood pressure in a carotis and the action potentials of splanchnic afferent fibres from the dorsal root /D 9 or 10/ or from truncus sympaticus /D 9 or 10/ were simultaneously recorded during left afferent splanchnic nerve stimulation in cats, immobilised by gallamine /Remolan/ before and after the administration of Pentobarbital /20-4omg/kg body weight. In non-anaesthetized cats, the splanchnic stimulation produces a decrease or an increase in blood pressure, depending on the parametres of stimulation. The activation of $\gamma\delta$ afferents /40-25m p.sec./ at frequencies of 5-10 p.sec. The activation of the slower δ fibres at frequencies 5-10 p.sec.brings about a depressor response, converted into a pressor response after Pentobarbital. The activation of the same fibres at 50-100 p.sec.elicits a pressor response unaffected by Pentobarbital, which also does not influence the pressor response, elicited by the total activation of the slowest δ and B splanchnic afferent fibres at all frequencies used.

NEURAL ORIGIN OF CARDIOVASCULAR REFLEXES FROM THE INTESTINE. M. H. Frank. Department of Physiology, New York Medical College, New York, N.Y. U.S.A.

The isolated vascular supply of innervated segments of ileum in urethane-anesthetized cats was perfused by a warmed oxygenated, electrolyte-glucose solution containing 2% of fresh beef red cells. Systemic increases of arterial pressure, heart rate and respiration occurred upon injection of acetylcholine or nicotine into the perfusion inflow. Vascular isolation, as well as abolition of responses during cooling of the nerves between torso and perfused organ, showed these reactions to be reflex. Reflex responses to 10-20 µg acetylcholine were sometimes abolished by prior injection of 10-100 µg atropine into the perfusion inflow, while similar responses to 10-20 µg nicotine were unaffected by 250 µg atropine. Reflex responses to acetylcholine were always accompanied by intraluminal pressure rises in the perfused segment (up to 200 mm Hg, air-filled balloon). Reflex responses to nicotine were accompanied by intraluminal pressure rises of -3 to +70 mm Hg. Atropine abolished these local pressure rises to acetylcholine and nicotine, although in three experiments abolition of the local responses to acetylcholine was accompanied by little or no diminution of the reflex responses. The reflex responses to these agents were thus separable from the local motor effects, indicating that they were due, at least partially, to direct stimulation of afferent nerve fibers. (Supported by the New York Heart Association).

FREQUENCY MODULATED ULTRASOUND TRANSIT TIME TECHNIQUE FOR MEASUREMENT OF BLOOD FLOW. D. Franklin, S. Kemper, T. Patrick, S. Vatner. Scripps Clinic & Res. Fndn. & U.C. San Diego Med. Sch., La Jolla, Calif., U.S.A.

Blood flowmeters measuring the differential transit-time of sound propagated through the blood have been complex, bulky and marginally stable. We have developed a new technique which overcomes these limitations: linear frequency modulated (nominally 10 MHz, \pm 150 kHz, 1 kHz repetition rate) sound is propagated between two piezo-electric crystals simultaneously upstream and downstream diagonally through the moving blood. At each crystal, two electrical signals occur: the projected signal and the signal arriving from the opposing crystal. The two signals differ in frequency by an amount proportional to the transit time of the sound travelling through the blood. The signals at each crystal are mixed and the difference frequency (about 30 kHz) signals are extracted. The phase difference between the two 30kHz signals is related to blood velocity (about 1 degree/cm/sec). The difference in phase is recorded in terms of blood velocity and volume flow. Advantages over previous ultrasonic transit time flowmeters include elimination of multitransit acoustical signals (reflection), and a common signal source, both of which improve stability significantly. Electrical shielding between the transducers is not required. The flowmeter is simple, is constructed in a small package, requires extremely low power (< 1 watt) and provides a stable and directional measurement of flow. These features in combination with the advantages of easily fabricated light weight transducers suitable for long-term implantation make this new instrument uniquely suitable for radio telemetry of directional phasic blood flow from unrestrained conscious animal preparations.

A MODEL FOR THE DYNAMIC RESPONSE OF SLOWLY ADAPTING MECHANORECEPTORS. G. N. Franz and D. G. Frazer. Dept. of Physiology and Biophysics, Univ. of Washington, Seattle, Wash. and West Virginia Univ. Med. Ctr., Morgantown, W. Va. U.S.A.

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The model takes account of the following experimental facts: (1) isotonic (isometric) deformation of tissues leads to creep (stress relaxation) responses proportional to log t (-log t). (2) Isotonic (isometric) deformation of slowly adapting mechanoreceptors causes adapting transients of generator potential and firing frequency which are proportional to the power function t-m (t-n; n>m) which can be approximated by a sum of several decaying exponentials. (3) Direct stimulation by constant currents leads to transients with at most one exponential. (4) The transient response not only reflects deformation and deformation rate (velocity) but also higher order derivatives of deformation (acceleration, etc.). (5) Transient responses to positive and negative deformation increments can by asymmetrical. The model assumes different rates for the logarithmic transients of the substrate tissue and the tissue coupling the receptor to the substrate. This leads to a transient of the form t-a for the membrane conductance as the surface area of the receptor membrane is altered by the deformation. As a result of the properties of the equivalent circuit for the receptor ending and of the spike generator, the transients for generator potential and firing frequency will be of the form t-m.

CHANGE IN ESTERIFICATION AS A REGULATOR OF FATTY ACID MOBILIZATION.

Bertil B. Fredholm. Dept. Pharmacology. Karolinska institutet. 104 o1

Stockholm. Sweden.

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Stimulation of the sympathetic nerves to canine subcutaneous adipose tissue with frequencies considered to be within the physiological rate of firing causes a release of approximately equimolar amounts of FFA and glycerol. Thus about 70 percent of the fatty acids formed are re-esterified. The re-esterification is correlated to the degree of glucose uptake, and an increase in the rate of glucose uptake by insulin will frequently increase the re-esterification. Re-esterification is furthermore increased by lactate in concentrations that occur during severe muscular exercise (above 7 mM), whereas pyruvate has the opposite effect. Another cytoplasmatic redox pair, malate and oxaloacetate, also have opposite actions on re-esterification. It is suggested that the cytoplasmatic NADH/NAD+ratio determines the degree of re-esterification, possibly by altering the degree of triosephosphate conversion into glycerolphosphate. The results demonstrate that the mobilization of fatty acids from adipose tissue can be considerably altered without any changes in lipolysis.

STABILIZATION OF TIDAL VOLUME WITH CHANGES IN MECHANICAL LOAD.

E. Kafer, J. Milic-Emili, J.M.B. Hughes and B.J.B. Grant.

Royal Postgrad. Med. Sch., London, U.K.

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In recent studies, Pengelly, Lynne-Davies and Milic-Emili found that during elastic loading the reduction in volume of the first loaded breath could be predicted from equations incorporating the stabilising effects of the intrinsic properties of the respiratory muscles. We have studied the effects of inspiratory resistive loading in normal human subjects at various levels of PCO₂ and found that tidal volumes on the first loaded breath were greater than would be predicted from Pengelly's simple model. Comparison of the effects of both elastic and resistive loading in the same subjects confirmed this apparent discrepancy. We have developed an alternative model based on the actual waveform of breathing rather than on a sinusoidal pattern as in Pengelly's model and using this, we could resolve the discrepancy and accurately predict changes in tidal volume with both types of load. Little change in the response to resistive loading was seen when normal subjects were anaesthetized with pentobarbitone or when the cervical vagi were cut or blocked in anaesthetized dogs. Our results suggest that intrinsic muscular, rether than reflex, mechanisms play the major role in the immediate compensation for changes in mechanical load.

EFFECT OF AMBIENT TEMPERATURE AND DURATION OF COLD EXPOSURE ON POST-COLD DRINKING RESPONSE OF RATS. M.J. Fregly and L.O. Lutherer, Dept. Physiol, Univ. Fla., Gainesville, Fla., USA

When rats are returned to a neutral ambient temperature following exposure to 5-6°C.air, an increase in spontaneous water intake occurs within 30 minutes and continues for at least 3 hours. Up to 10% of the 24 hour fluid intake may be ingested within one-half hour. test the effect of both temperature and duration of exposure on post-cold (P.C.) drinking response, four separate groups of rats were exposed to 5.0, 7.5, 10.0 and 13.0°C. for 9 days. Food and water were available ad libitum. Controls for each group were maintained at 26°C. The rats were removed from cold after 1, 3, 6 and 9 days. Both experimental and control groups were immediately offered cold water to drink and water intakes measured hourly for 3 hours. The maximal ambient temperature at which a P.C. drinking response was obtained following a 24 hour cold exposure was 10.0°C. After 3, 6 and 9 days of cold exposure, P.C. drinking increased significantly only in the group previously exposed to 5.00C. Thus, the stimulus inducing P.C. drinking was gone after 3 or more days of continuous exposure to 7.50C or higher, but not to 5.00C. An increase in serum osmolality, a reduction in the ratio of water to food intake and an increase in the ratio of urine output to water intake accompany exposure to $5-6^{\circ}$ C. Thus, the P.C. drinking response may result from cold-induced dehydration. Explanation for the dehydration, as well as the failure of cold-exposed rats to drink enough water voluntarily to prevent dehydration, awaits further study. (Supported by Contract N00014-68-A-0173-0007 with the Office of Naval Research).

545 SCORPION TOXIN, AN IMPORTANT TOOL FOR PHYSIOLOGICAL RESEARCH. L. Freire-Maia, V.P. Costa Val, W.L. Tafuri, A.D. Azevedo, T.A. Maria, J.R. Cunha Melo, G.I. Pinto and I. Franco. Dept. Fisiologia ICB, UFMG, C.P. 2486, Belo Horizonte, Brasil.

Purified toxin fractions obtained from Brazilian scorpion <u>Tityus serrulatus</u> produce interesting physiological effects in anesthetized rats: 1) Sinusal bradycardia, sino-atrial and A-V block, ventricular ectopic beats, ventricular paroxistic tachycardia. These effects are assumed to be due to the simultaneous release of acetylcholine and catecholamines; 2) Hypertension, due to the release of catecholamines from adrenal glands and postganglionic nervous endings; 3) Gasping and ataxic breathings (Freire-Maia et al., 1970). These effects did not occur in rats in which the carotid bodies regions were desnervated and the vagi cut. On the isolated rat ileum, toxin produced both contractions and relaxations, due in part to release of acetylcholine and catechomines. Electron microscopic studies have shown that toxin causes a pronounced alteration of the vesicular components of the myenteric plexus (decrease in dense and increase in agranular vesicles).

546 INTERACTION OF PRESSOR RESPONSES WITH HYPOTENSION DUE TO STIMULATION OF THE SEPTAL AREA*. A. Freitas da Rocha, and C. Timo-Iaria. Dept. Physiol. Pharmacol., University of São Paulo, São Paulo, SP, Brazil.

Stimulation of the septal area provokes a fall in blood pressure and inhibits the beroreceptor reflex (Covian, M.R., and Timo-Iaria, C., Physiol. Behav. 1966, 1:37-43). 1. A systematic study of the pressor responses to bilateral carotid occlusion and to stimulation of somatic afferents in the sciatic nerves of the cat during septal hypotension showed that both reflexes are inhibited. 2. This was found to occur even when the septal effect was small, and sometimes overlasted it. 3. Lesion of the dorsal midbrain tegmentum did not alter the hypotensive effect but released the pressor responses previously inhibited. 4. Total destruction of the dorsal midbrain tegmentum and partial lesions in the ventral tegmentum did not abolish the septal hypotension. 5. Only bilateral destruction of the ventral tegmentum suppressed it. The described results show that septal area stimulation provokes hypotension and blocks pressor responses using different pathways.

*Supported by the State of São Paulo Research Foundation (FAPESP).

AN INVESTIGATION OF THE POSSIBLE TRANSPORT ACTIVITY OF AMMIOTIC EPITHELIUM. C.J. French, M.B. Segal and Pat. M. Foreman. Sherrington Sch. Physiol. & Dent. Gynaec. St. Thomas's Hosp. Med. Sch. London S.E.1.

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The amniotic membranes have been suggested as a possible site of formation of the amniotic fluid and although Garby (1957) was unable to demonstrate active transport in vitro, French, Maclennan & Wynn (1971) have shown that there is a specific localisation of Na,K activated ATPase in the intercellular clefts of the amniotic epithelium. The ultra structure of the amnion is similar to that of other transporting epithelia and Diamond & Tormay (1966) have proposed that this type of cleft is the site of transepithelial fluid transport, water following an osmotic gradient established within the cleft by the active transport of Na into the region close to the tight junction.

It was thus of interest to repeat the in vitro experiences using an Ussing type apparatus and measuring the flux of Na in both directions simultaneously with isotones, and the transepithelial potential difference. As yet no potential has been demonstrated nor may not be involved in fluid transport. Keynes (1959) has pointed out that the detection of ATPase activity is not an index of transepithelial sodium transport, but possessed by all cells to maintain the intracellular environment. However, the finding of this specific localisation of enzyme is puzzling if it is only related to the above activity. Further studies are in progress using guinea pig, sheep tissue to investigate this problem.

INVESTIGATION OF ADRENAL SENSITIVITY TO ACTH IN REGULAR MUSCULAR ACTIVITY R.Frenkl, L.Csalay, G.Csákváry. Pathophysiological Institute, Semmelweis Medical University, Budapest, Hungary.

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Previously the authors found that 1. the effect of ACTH as measured by the rise of plasma steroid concentration did not differ in rats trained by 6 weeks of swimming and in humans engaged in regular sports activity from that observed in controls; 2. plasma steroid level increase in response to a familiar exercise was less in trained animals and humans than in controls; 3. steroid elimination was accelerated in animals trained by swimming. - In the present experiments it was shown that in vitro adrenal sensitivity to ACTH of animals trained by swimming was higher than that of controls. This phenomenon developed relatively soon in the course of training /by the second or third week/ and was maintained still when the rise of peripheral steroid level due to exercise already became slight. These results support the conception that ACTH secretion when elicited by an exercise, is less in the trained organism. In the change of adrenal cortical activity it is regular swimming proper and not the manipulation associated with it that is of primary importance.

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LATENCY DIFFERENCES BETWEEN INHIBITION OF OFF-CENTER NEURONES AND EXCI-TATION OF ON-CENTER NEURONES. H.-J.Freund, C.Wita, R.Brüstle. Abteilung für Neurophysiologie, Universität Freiburg, BRD Following incremental light stimuli the latencies of inhibition of

Following incremental light stimuli the latencies of inhibition of off-center neurones were compared to that of excitation of on-center neurones in extracellular recordings from optic tract fibers of N₂O-anaesthetized cats. The receptive field centers were illuminated by small light spots of different intensity. Stimulus size was a fixed portion of the area of the receptive field center. Background illumination was 5 asb. For all intensity levels, the latencies for inhibition of off-center neurones were significantly shorter than for excitation of on-center neurones. Most off-center neurones were inhibited completely, before the fastest on-center neurones of the sample were excited. The magnitude of the latency difference depends upon the previous activity of the neurones. The results agree with those of LICKER for rabbit retinal ganglion cells and of TOYODA for fish bipolar cells. Thus, considering the two neuronal subsystems B (on-center neurones) and D (off-center neurones) as antagonistic information channels, the inhibition of the D-system is the first reaction of the visual system to incremental light stimuli. The meaning of this phase difference between the two neuronal subsystems for sensory information processing is discussed.

PARATHORMONE AS A MEDIATOR OF INORGANIC PHOSPHATE DIURESIS DURING SALINE INFUSION IN THE RAT. A.Frick, Dept. of Physiology, Univ. of Aachen, Germany.

Clearance methods were employed to study the mechanism of inorganic phosphate diuresis during saline infusion in the rat. When normal rats were infused with isotonic saline (0.50 ml/min for 2 hr), they excreted 12.9 \pm 0.7% of filtered sodium (mean \pm S.D.), but at the same time as much as 38.8 \pm 3.0% of filtered phosphate (n=8). The addition of calcium and magnesium in combination to the infusion solution decreased fractional phosphate excretion significantly to 11.2 \pm 3.6% (n=10), while sodium excretion was unchanged. When parathyroidectomized rats were infused with isotonic saline (0.50 ml/min for 2 hr), fractional phosphate excretion was only 0.9 \pm 0.9% (n=10), whereas simultaneous sodium excretion was similar as in the controls. Administration of parathormone (Lilly) to saline infused parathyroidectomized rats resulted in marked increases in inorganic phosphate excretion to 41.5 \pm 3.1% of filtered phosphate (n=10), sodium excretion, however, again remained constant. It is concluded from these results, that saline induced phosphaturia in normal rats is mediated primarily by parathormone. Sodium excretion under these conditions appears to be independent of changes in parathyroid activity and of changes in inorganic phosphate excretion.

EFFECTS OF CHEMOPALLIDECTOMY AND CHEMONIGRECTOMY ON CAUDATO-THALAMIC EVOKED ACTIVITIES. T.L. Frigyesi, A. Iulo, F.V. Exconde, R.A. Troiano, and B.M. Rigor. Parkinson's Disease Res. Ctr., Col. of Physicians & Surgeons, Columbia Univ., New York, N.Y., USA.

Low-frequency (8/sec) stimulation of the head of the caudate nucleus (Cd) elicits brief (20-30 msec) excitatory and prolonged (80-100 msec) inhibitory effects in thalamic relay neurons of the cerebellum-motor cortex projection system. Intracellular recordings have revealed that such Cd stimulation produces sustained hyperpolarization in neurons in the medial pallidal segment which generally prevent Cd evoked EPSPs to attain firing level. Consequently, pallidothalamic fibers (ansa and fasciculus lenticularis) are only conditionally available to caudato-thalamic projection activities. On the other hand, Cd stimulation monosynaptically activates substantia nigra neurons which, in turn, elicit monosynaptic EPSPs and EPSP-IPSP sequences in thalamic neurons. Furthermore, chemopallidectomy (produced by intranuclear administration of manganese) did not but chemonigrectomy (produced by intranuclear administration of 6-OH dopamine) did abolish the Cd evoked EPSP-IPSP sequences in thalamic neurons. These data indicate that caudatofugal activities mostly utilize relays in substantia nigra to gain access to thalamic neurons; caudato-nigro-thalamic projection activities exert powerful regulatory effects in the thalamic relays of the cerebellum-motor cortex projection system. (Supported by NINDS Grant #NS 09017-01.)

DETERMINATION OF EFFECTIVE CAPILLARY PRESSURE IN THE ISOLATED DOG LIMB BY AN ISOCONDUCTOMETRIC TECHNIQUE. A. Fronek, AMES-Bioengineering, School of Medicine, University of California, San Diego, La Jolla, Calif. 92037.

In analogy to Pappenheimer and Soto-Rivera's isogravimetric technique, the effective capillary pressure was determined by continuous monitoring of electrical conductivity of effluent blood. Inflow and outflow pressures were controlled to obtain an isoconductometric state (no change in electrical conductivity). The flow values were plotted against the corresponding isoconductometric venous pressures and the effective capillary pressure was obtained by extrapolation to flow = 0. The mean value of experiments on 15 dogs was 25.5 ± 7.17 mm. Hg. The results were compared to those obtained by the isogravimetric (Pappenheimer-Soto-Rivera) and zero-flow (Johnson) technique and no statistically significant difference was found. It seems, therefore, that this technique is suitable for effective capillary pressure determination without the requirement of an isolated preparation and continuous weight monitoring. (Supported by a NHLI Grant, HE-12690.)

CONCENTRATION DEPENDENCE OF SMALL SIGNAL MEMBRANE CONDUCTANCE IN THE OUTER RESISTIVE MEM-BRANE OF FROG SKIN. W.Fuchs, U.Gebhardt, N.A.Nacimiento, and B.Lindemann, 2nd Department

Isolated skin of Rana esculenta was equilibrated with gluconate-Ringer on its inner and with 10 mM Na-, 1 mM Ca-gluconate on its outer surface. By means of a rapid flow device, the outer solution was replaced by a test solution of different ionic composition for pethe outer solution was replaced by a test solution of different ionic composition for periods of 0.1 - 2.0 s, while the change of P.D. and skin conductance (g) was recorded. With increasing (Na)_o, g saturates at a plateau level g_{Na}^P which is about twice the plateau level g_{Na}^P reached with increasing (K)_o. Both levels are reached when concentrations have been increased to 10 mM. g is 10 % smaller than g_{Na}^P when the test solution contains both Na and K in concentrations of 10 mM. A further depression of g is observed when (K)_o is increased

much above (Na) . After adding Amiloride to the outer solutions (0.8 - 8 mg/l), g_{Na}^P and g_{K}^P become almost equal and slightly smaller than the control value of g_{K}^P .

The results can be explained with two types of saturable parallel transport channels, A and B, with permeabilities

we assured with either Na or K in the outside solution in equal concentrations. Large (K) may depress g by lowering P_{Na}^A , while Amiloride may depress g by reducing P_{Na}^A and P_{K}^A to zero. (Supported by the Deutsche Forschungsgemeinschaft, SFB 38)

LACRIMAL SECRETION FLOW BEFORE AND AFTER CUTTING THE LACRIMAL NERVE. N.Fuenmayor.Dept. of Physiology, Sch. of Med., Univ. of Zulia, Maracaibo,

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In male anesthetized rabbits the lacrimal secretion flow was estimated by collecting the fluid coming from the excretory duct of the right inferior lacrimal gland in polyethelene precalibrated cannulae in a given time both during control and stimulation periods. The lacrimal nerve (intact or cut) was stimulated by means of square electrical pulses(25 pulses/sec., cut) was stimulated by means of square electrical pulses(25 pulses/sec., and 0.5 msec. in duration) at varied voltage(3,5,8,10,25 and 35 volts) through chlorided silver electrodes. Results(mean and standard error) show a control lacrimal fluid flow of 0.17+0.02 uL/min., N;6, which decreased significantly when the nerve was $\operatorname{cut}(\overline{0.09+0.01}$ uL/min., N:6). During the stimulation period the lacrimal fluid flow increased up to a maximun of 10.20+1.96 uL/min, N:6(intact nerve) and 3.25+0.95 uL/min., N:6(cut nerve) obtained with a stimulation of 25 volts. These flindings show a significant depression in the lacrimal secretion when the lacrimal nerve was cut which depression in the lacrimal secretion when the lacrimal nerve was cut which was greater during the stimulation period. This could indicate that the lacrimal secretion is partially reflex during the control period, and mainly mediate by a reflex mechanism during nervous stimulation.

IMPROVED METHOD FOR ELECTRICAL ACTIVITIES OF BRAIN SLICE IN VITRO AND ITS APPLICATION TO THE OLFACTORY CORTEX. T. FUJII AND Y. IWASE. Dept. of Physiology, Kyoto Prefectural Univ. of Med., Kyoto, Japan.

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The brain slice, placed on the nylon mesh in the middle of a funnel, was perfused with the medium at a constant flow rate and blown up with 95% 02+5% CO2 gas mixture through the funnel stem (gas-blow and medium-flow method). This procedure enabled us to record stably electrical activities from slices for about 6 hours and made it easy to exchange the media with different constituents. Using this method, olfactory cortex responses were studied by the lateral olfactory tract (LOT) stimulation in guinea pigs. The response is serially composed of the initial spike (IS) representing impulses of LOT axons, negative (N) and positive (P) potentials. The N potential probably indicates the reflection of EPSPs evoked on the apical dendrite of the superficial pyramidal cell, while the P potential means reflection of IPSPs on soma and trunk of apical dendrites of the pyramidal cell. Glycine, β-alanine and GABA had no effect on the N potential at concentrations less than 5x10°M.

The P potential decreased in amplitude at 10°210°M of these drugs and such an effect of GABA was solely competed with strychnine suggesting that GABA might be a transmitter in inhibitory synapses in the olfactory tubercle.

STUDIES ON EXAGGERATED KNEE-JERK IN CHRONIC SPINAL HEMISECTED MONKEYS. B.Fujimori and M.Aoki. Dept.of Physiology, Hokkaido Univ., Sch.of Med., Sapporo, JAPAN.

As an extension of the study of spasticity following spinal hemisection in the cat (Nobel Symposium 1, 1966), spinal hemisection(Th8) was carried out in 18 monkeys. Various kinds of "clinical" examinations for spasticity were made and the behavior was also observed for 2-13 weeks after the hemisection. (1) The most distinct and common(15/18) phenomenon was the marked exaggeration of the knee-jerk on the hemisected side which developed gradually 2-3 weeks after the hemisection. It is noteworthy that this phenomenon still remained during the flaccid palsy following Nembutal(25 mg/kg) i.v. administration or even after the total spinal transection 1 segment below the hemisected site. (2) Experimental results of monosynaptic reflex responses by stimulation of the quadriceps nerve, such as input-output relation curve, effects of repetitive stimulations of the nerve, were in accordance with above noted clinical phenomenon on the hemisected side. Intracellular microelectrode experiments are under study. (3) Nauta's histological observations of the lumbar cord revealed that degenerated fibers were observed in the intermedial site and close to or even in the ventral collumn besides the pyramidal tracts on the hemisected side, but also on the contralateral side to some extent. (4) Spontaneous movements of the flaccid hindlimb began 3-5 weeks after the hemisection in all cases. Therefore this mechanism is also the purpose of the present experiment.

PHYSIOLOGICAL PROPERTIES OF SINGLE FIBER FROM FROG SKELETAL MUSCLE UNDER THE INFLUENCE OF HYPERTONIC UREA-RINGER WITH PARTICULAR REGARD TO THE STRUCTURAL FLEXIBILITY OF TRANSVERSE TUBULAR SYSTEM. M.Fujino. Dept. of Physiology, Sapporo Medical College, Sapporo, Japan.

Our early observation (Nature 192: 1159, 1961) has shown that, after the completion of immersion in a hypertonic glycerol-Ringer, fibers of frog skeletal muscle give a selective inhibition of contraction in presence of action potential (a type of 'glycerol effect'). The phenomenon is at present considered to be due to a disruption of transverse tubules. The present communication deals with such a problem on urea done in this decade Frog skeletal muscle was used. (1) If a fiber is immersed in hypertonic urea-Ringer, twitch is abolished and then reappears (sometimes disappears again); when normal Ringer is restored, action potential without contraction occurs. (2) This after-potential diminishes at the time when the fiber becomes less transparent and loses the twitch ability (3) In this phase, the tubules are recognizable and opened at fiber surface, but narrow. Conclusion: (1) electrotonic spread inwards of electric events on fiber surface depends on the tubular diameter; (2) the tubules are flexible, can swell or shrink (extremely, disappear); (3) for the shrinkage, the pretreatment with non-electrolyte seems to be necessary.

PHASIC AND TONIC DISCHARGES IN THE CAT'S OPTIC NERVE AND LATERAL GENICULATE BODY. Y. Fukada and H. Saito. Res. Group on Auditory and Visual Information Processing, NHK Broadcasting Science Res. Lab., Kinuta, Setagaya-ku, Tokyo, Japan.

Cat's optic nerve fibers having either on- or off-center receptive field were further classified into two types; Type I (phasic) and Type II (tonic). Type I responded to only a transient increase or decrease in the luminance of the stimulus, while Type II continued to respond to a stationary light spot or a small black object. The conduction velocity of Type I fibers was faster, on the average, than Type II. In the lateral geniculate body (LGB), discharge patterns of the single units to the photic stimulation at the center of the receptive field were analyzed, and latencies were compared between the responses to the stimulation of the visual cortex and optic chiasm with the same units. As a result, cells with center-surround receptive field could be similarly categorized. LGB units which showed transient "on" or "off" responses to the onset or cessation of light spot responded to optic chiasm stimulation with a relatively short latency (less than 2 msec). They were also activated antidromically by stimulation of the visual cortex with a relatively short latency (less than 1 msec). On the other hand, units responding with sustained discharges to the light spot or to a small black object showed relatively long latencies both to optic chiasm and to visual cortex stimulation. Above results suggest that the characteristics of Type I and Type II in the optic nerve are taken over by LGB cells.

EFFECTS OF PROSTAGLANDIN E $_2$, ON RENAL TUBULAR REABSORPTION OF SODIUM AND FLUID IN RATS. $\underline{\text{G.FÜLGRAFF}}$, Dept. of Pharmacology, T.H. Aachen, Aachen,

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I. v. infusions of PGE, in saline at rates of 10, 50, 100 and 200 ng/100 g rat weight · min enhanced urine output, urinary sodium concentration and sodium excretion rate dependent. Fluid and sodium excretion increased dumaing the first 60 min after the onset of the infusion of PGE, and remaximal effects are observed at 100 ng/100 g · min and up to this rate no decreased. Quantitatively the increase at 100 ng/100 g · min blood pressure 330% in urine volume, 290% in urinary Na concentration and 960% in Na exwas not characteristically affected. Micropuncture experiments indicated nished according to measurements of TF/P_T and TF/P_T. Proximal transit time was equally not influenced. Experiments on distal fractional reabsorption experiments are still going.

SPECIFIC ALDOSTERONE BINDING PROTEINS IN RAT KIDNEY AND PAROTID. J. W. Funder, D. Feldman, D. Goodman, and I. S. Edelman. Cardiovascular Res. Inst., Univ. of California

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Specific 3H -aldosterone binding proteins were isolated from (1) cytosol by G-50 sephadex chromatography, (2) nuclear fractions by Tris-CaCl $_2$ extraction and 50% (NH $_4$) $_2$ SO $_4$ precipitation (soluble nuclear), and (3) nuclear fractions by 0.4M KCl extraction and 50% (NH $_4$) $_2$ SO $_4$ precipitation (chromatin bound). In each of these three compartments, the time-course of specific aldosterone binding has been determined by 0-4 hours incubation of rat kidney slices with 3H -aldosterone. Cytosol ABP binds 3H -aldosterone rapidly over the first 20 minutes of incubation; thereafter levels of specifically bound 3H -aldosterone remain constant. Soluble nuclear ABP uptake of 3H -aldosterone is linear with respect to time; until 3H 00 minutes incubation lower than that of ABP, thereafter higher. Also linear is the specific binding of 3H -aldosterone to the 0.4 M KCl extractable nuclear fraction, but with a lower specific activity than to the Tris extractable fraction. Cycloheximide (0.5 μ g/ml) was without effect upon the extent or time-course of specific 3H -aldosterone binding. Similar studies upon rat parotid gland have shown similar but not identical patterns of specific 3H -aldosterone binding; in this tissue the chromatin bound ABP appears of higher specific activity than its counterpart in the kidney.

THE EFFECT OF VAGAL STIMULATION ON THE HEART OF THE DOG, DUCK AND TOAD. C. M. Furnival, R.J. Linden and H. M. Snow, Cardiovascular Unit, Department of Physiology, University of Leeds, England.

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Stimulation of the cervical vagus nerves in the dog, duck, and toad results in a decrease in heart rate but the evidence for a negative inotropic effect on the muscle of the left ventricle is controversial. The maximum rate of rise of pressure in the left ventricle (dP/dt max) has been shown to be a quantitative index of inotropic changes in a preparation in which the secondary inotropic effects of changes in heart rate and mean aortic pressure were prevented from occuring during the measurement of dP/dt max (Furnival, Linden & Snow, 1970). Stimulation of the vagus nerves resulted in a 39% decrease in heart rate and a 5% decrease in dP/dt max in the dog; a 48% decrease in heart rate and a 5% decrease in dP/dt max in the duck; a 49% decrease in heart rate and a 30% decrease in dP/dt max in the toad. It is concluded that whereas stimulation of the vagus nerves results in a significant negative inotropic effect on the ventricle of the toad there is no significant effect on the ventricle of the dog and duck. This conclusion supports the anatomical evidence suggesting that vagal nerves supply the ventricular muscle of the toad but not the dog and duck.

Furnival, C.M., Linden, R.J. & Snow, H.M. (1970). J. Physiol. 211, 359 - 387.

TRANSMITTER RELEASE FROM SENSORY HAIR CELLS IN GOLDFISH'S EAR. T. Furukawa and S. Matsuura. Dept. of Physiology, Osaka City Univ. Med. Sch., Abeno-ku, Osaka, 545 Japan. 562

In the sacculus of goldfish, i.e., the fish's inner ear, each sound wave serves as an individual stimulus to hair cells giving rise to a microphonic which is followed by an EPSP in afferent fibers with a synaptic delay of about 0.6 msec. Since responses of hair cells are graded, giving a tone pip stimulus to fish's ear is equivalent to giving repetitive depolarizing pulses to presynaptic elements paralyzed with tetrodotoxin in other Present study is concerned with a rundown of EPSP's; successively evoked EPSP's were reduced in size keeping approximately a constant ratio of about 0.6 to the preceding ones, suggesting that the phenomena could be attributed to a depletion of readily available transmitter store. (No comparable decline was found in the microphonics.) Moreover, the (No comparable decline was found in the microphonics.) decline took place approximately at the same rate for different intensities of sound, suggesting that the size of readily available store would vary as a function of the magnitude of presynaptic depolarization. When the saccular macula was perfused with solutions rich in Mg ions, EPSP's were generally reduced in size, but the rundown rate became slower. A perfusion with solutions rich in Ca ions showed an opposite effect, suggesting that the Ca-Mg ions in the medium mainly affect the "release factor".

BLOOD GLUCOSE LEVEL IN PREGNANCY. Y. Gabr, M.H. Ghanem, M.El Abd, N.A. El Dardiry. Med. Res. Inst., Alexandria, and Faculty of Med., Alexandria Univ., 563

A battery of tests has been carried out on three groups of pregnant A battery of tests has been carried out on three groups of pregnant cases: normal, prediabetic and frank diabetic cases. The changes in blood glucose level of these pregnant cases, as a result of oral glucose, intravenous insulin-glucose, further fasting for four hours, and tolbutamide intake, have been studied. The levels of serum inorganic phosphorus, serum potassium, serum alkaline phosphatase, and serum protein pattern of these cases were also determined. The results obtained show that there is increased insulin secretion in pregnancy. The prediabetic pregnants show hyperinsulinemia which becomes evident during fasting and after tolbutamide intake. Liver function is also stressed, the stress being more marked in intake. Liver function is also stressed, the stress being more marked in the diabetic group.

564 PREDICTION OF HUMAN BODY TEMPERATURE DURING MAXIMAL EXERCISE FROM SKIN, RECTAL, ESOPHAGEAL AND MUSCLE TEMPERATURES. A.P.Gagge and B.Saltin. J.B.Pierce Lab., New Haven, Conn., USA.

Three normal unclothed subjects exercised to exhaustion with maximal work loads at ambient temperatures $10^\circ-40^\circ\text{C}$ (rh $\sim40\%$). During the exercise and recovery phases mean body temperature $\overline{T}b$ was determined by integrating the change $\Delta \overline{T}b$, calculated each minute from the heat storage S, given by the equation $S=M-W-E-h(\overline{T}sk-Ta)$ in W/m^2 , where metabolism M, work W, evaporation E, Tsk, as well as Tre, Tes and Tm were measured continuously. During rest on bicycle ergometer h=9.23 W/($m^2 \cdot ^{\circ}$ C) and for exercise at 60 rpm h=11.23. Integration began five minutes before start of exercise; the initial Tb was estimated from average of Tsk and Tes weighted by 1:4. The following regressions were observed:

Phase	Multiple Regression	R ²	SEE
Exercise and recovery	$\bar{T}b = 0.20 \; \bar{T}sk + 0.94 \; Tes - 4.51$	0.84	±0.29
Exercise Exercise	Tb = 0.22 Tsk + 0.57 Tre + 0.34 Tm - 4.00 Tb = 0.21 Tsk + 0.51 Tes + 0.24 Tm - 1.97	0.96	±0.14 ±0.15
Recovery	Tb = 0.22 Tsk + 0.99 Tes - 7.13	0.81	±0.31
R = corr	elation coef.; SEE = std. error of estimate		

In general, during exercise $\Delta \overline{T}b$ may be estimated from the observed $\Delta \overline{T}sk$ and ΔTes when weighted 1:4.5.

CIPCADIAN CONTROL OF CARBOHYDRATE AND PROTEIN METABOLISM IN MUSCLE. J.J.Ga-gliardino, M.T.Pessacq and O.R.Rebolledo. Inst.of Physiology, Sch.of Med., Univ.of La Plata, Argentina.

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The existence of a circadian control upon several metabolic processes has been clearly demonstrated in manmals. We have studied the C-14-leucine incorporation into protein as well as the glycogen synthesis in diaphragm hoth in vivo and by the incubation technique at different time points of the day. Female mice kept in a cycle room with light-darkness periods of 12 hs. each were used. The experiments were performed at intervals of 4 hs. each. Both processes showed a clear circadian pattern either <u>in vivo</u> or <u>in</u> with higher synthetic rates occurring during the resting period(06:00 -18:00) and the lowest values located within the activity one(18:00-06:00). Furthermore, when the effect of insulin upon protein and glycogen synthesis was tested, a 24 hs. response curve was also obtained. The simultaneous study of the scrum glucose and immunoreactive insulin levels in the animals during a circadian cycle offered a guide for the interpretation of the above-described changes. These results strongly suggest that the perfornance of this type of dynamic metabolic studies, following a circadian scheme, should provide a helpful key for interpretation of muscle metabolic

AUTORHYTHMIC BEHAVIOUR AND CONSTRICTORY RESPONSES IN THE SIMULTANEOUSLY PERFUSED ARTERY AND VEIN OF THE ISOLATED RABBIT EAR. S.Gagov, K.Hartmann, W.Herbst, H.L.Thron. Inst.Klin.Physiologie, Freie Univ., Berlin 45,Germany

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There is evidence from recent studies in different vascular beds (e.g. the rabbit ear), that the contractile behaviour of arteries and veins to the same vasoactive stimulus may differ markedly. In order to investigate whether this holds true also with respect to autorhythmic activity (ARA) of both kinds of vessels, especially when studied under identical conditions, the response pattern of simultaneously perfused in situ segments of the central artery and the marginal vein from the isolated skinned rabbit ear to vasoactive substances, to changes of K⁺ and Ca⁺⁺ concentrations in the perfusate, and to changes in the temperature level was examined. Both vessel segments were cannulated and artificially perfused by the same test solution and constant driving pressure; flow and flow resistance were measured separately. - Though generally not observed with Tyrode solution, ARA regularly could be induced by catecholamine infusions (> 10-8 g/ml). The rate of basic rhythm markedly increased when temperature levels changed from +12 to 41°C, but was rather stable when K⁺ or Ca⁺⁺ concentration amounted up to 10 mEq/l. There was no strict correlation between the constrictory responses of either vessel and the parameters of autorhythmic activity.

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TRANSMITTER MOBILIZATION AT THE MAMMALIAN MYONEURAL JUNCTION - TEMPERATURE EFFECT.

A. Galindo. University of Washington School of Medicine, Dept. Anesthesiology & the Anesthesia Research Center, Seattle, Wash. 98105 (Supported by USPHS Grant GM 15991-03).

The Q10 (38-20°C) of transmitter mobilization was studied by intracellular recording from end plates of unparalyzed rat diaphragm preparations. Mobilization of transmitter was calculated indirectly from end plate depolarization in mV/second. Determinations were made during a steady state plateau of end plate potential (epp) amplitude induced by tetanic stimulation (1 to 200 Hz) of the phrenic nerve. Transmitter mobilization, expressed as a fraction of the transmitter pool, was linearly related to frequency of stimulation at 32°C. The size of the transmitter pool was calculated from the first 8 to 10 epps (rundown) before steady state. Lowering of the temperature to 22°C depressed transmitter mobilization (> 40%). This depression was greater at higher frequencies of stimulation. However, owing to a 3-fold increase (1.73 msec to 6 msec) in the duration of the absolute refractory period of motor nerve terminals, mobilization of transmitter was seldom studied above 50 Hz at low temperature. These results support the hypothesized existence of a limited transmitter pool at the motor nerve terminal. Lowering the temperature affected mobilization rate, increased the duration of the absolute refractory period of motor terminals, blocked invasion of a number of motor nerve terminals by action potentials depending on the pressure applied to the preparation, increased amplitude of epps, and reduced amplitude and frequency of miniature end plate potentials.

THE ROLE OF GLOBUS PALLIDUS AND HIPPCCAMFUS IN THE FORMATION OF THE FUNCTIONAL SYSTEM OF BEHAVIOR. L.S.Gambarian, A.A.Garibian, J.S.Sarkisian, I.N. Koval. Lab. of Neurobionics Armenian Academy of Sciences, Yerevan, USSR.

In experiments carried out on cats, it has been shown that under special conditions of method partial destruction of the globus pallidus and hippocampus leads to a disturbance of the integration - in the process of afferent synthesis - of the capacity of simultaneous integration of the excitations: (a) from the starting stimulus (conditional signal), (b) from the situational stimulii (left and right feeders, pedals - the pressing of which enabled the cat to obtain food), and (c) from the apparatus of memory. Partial destruction of the pallidum leads to a rapid extinction of feeding and avoidance conditioned reflexes. In case of total bilateral destruction of the globus pallidus, the artificial conditioned reflexes disappear permanently. Electrostimulation of the pallidum leads either to a facilitation of conditioned reflex activity (2-2.5v, 50 hz, 0.5msec), or to an inhibition (5-6v, 50 hz, 0.5 msec) of the latter.

The results suggest that the pallidum and hippocampus have a close relationship with the mechanisms of learning and memory.

NEW DIMENSIONS IN ACID-BASE PHYSIOLOGY. J. L. Gamble, Jr. and J. A. Bettice. Department of Physiology, Johns Hopkins School of Medicine, Baltimore, Maryland, U.S.A.

Emphasis in teaching and in conceptual analysis in acid-base physiology is being placed less upon the red cell reactions and more upon those which provide buffering in the whole body. We have been inducing controlled respiratory changes in dogs during infusions of HCl to study:—A. Quantitative relationships in mixed (respiratory and metabolic) disturbances. As reported earlier (XXIV Internat. Congress) variations in pCO₂, 20-60 mm Hg, were not found to alter the distribution of buffering between intra- and extracellular compartments. In the acid in addition to the normal range respiratory-induced changes in the plasma bicarbonate were 1.1-1.3 mEq/liter for variations of 10 mm Hg in the pCO₂. If these values are used to correct for the respiratory effect, the decrease in the concentration of plasma bicarbonate becomes closely proportional to the excess of non-volatile acid in the body. B. Mechanisms of whole body buffering. Tissue (non-Blood) buffering of infused HCl, with Na-H exchange, could not be correlated with absolute changes in pH either in or out of the cell. This buffering has appeared to be associated with changes in the gradient of hydrogen ion concentrations across the cell membrane. The relationship differs from that in the red cell where non-bicarbonate buffering relates directly to change in extracellular acidity.

ORGAN RESPONSIBILITY, HOMEOSTASIS AND CONDITIONAL REFLEX FORMATION. W. Horsley Gantt. Pavlovian Lab., Veterans Administration Hosp., Perry Point, Maryland, USA.

Pavlov's CR has become an accepted stereotyped pattern: Unconditional stimulus (food) signal (bell), and presto! a salivary CR. This pattern has been applied to various organs with the assumption that all activity of any organ can become a CR, cardiac, salivary, renal, motor, etc. Seventy years after Pavlov, on the basis of our work with the kidney the applicability of this stereotyped pattern of CR formation is questioned. Diuresis does not become a CR. This negative experiment reveals that the function which an organ subserves in the body economy is the determining factor whether the activity will fall into the CR paradigm. For, if diuresis routinely became a CR, valuable electrolytes and water would be irrevocably lost when the signal failed to signalize intake; for urine once secreted into the renal pelvis can not be reabsorbed, unlike salivary and gastric secretions which are reabsorbed. Thus if there were a renal CR the body economy might be seriously unbalanced and schizokinetic. Organ-responsibility means that an organ-system can not be conditioned when this would lead regularly to imbalance and destruction of the living process. But we do not have to resort to universal teleology to explain each individual action—the organ-system may not discriminate among the values of separate acts within that organ-system—rather its general function is to maintain balance (homeostasis) and life. Often nonteleological events occur resulting in pathology. But CR formation does not occur when any CR in that system would be antihomeostatic.

THE EFFECT OF TENSION ON THE ULTRASTRUCTURE OF VERTEBRATE SMOOTH MUSCLE.

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Thick filaments were regularly found in smooth muscle cells of the guinea pig ileum, if the specimens were fixed at constant length higher than the excised length. Thick filaments consisting presumably of myosin were present also in stretched muscles relaxed by, and fixed in presence of atropine. It seems that both kinds of filaments are regular constituents of smooth muscle, but myosin filaments survive processing only when the cells are subject to mechanical tension. The fact that fixation may selectively annihilate myosin filaments could be demonstrated also on a striated muscle. Thus the lack of myosin filaments in unstretched smooth muscles does not support the concept of a reversible aggregation and disaggregation of myosin.

TENSION CHANGES BY DIFFERENCES IN THE SHAPE OF INDUCED MUSCLE ACTION POTENTIALS. H. García, R. Glancszpigel and O. Uchitel. Centro de Investigaciones Neurológicas. Instituto T. di Tella. Buenos Aires. Argentina.

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Muscle fibers of land-fresh water crab treated with procaine developed prolonged action potentials (A. P.) Analysis of various parameters of the A. P. and the parallel changes in tension established: i) a relationship between the duration of the plateau phase and duration of tension up to the maximum, ii) a relationship between the negative slope of the A. P. and rising phase of tension, and iii) that the maximal tension developed is a combined function of the duration of the A. P. and the negative slope of its plateau. External Ca++ seems to be responsible for the development of A. P. and mechanical output.

LOCAL RESPONSES IN THE DENDRITIC LAYER OF THE CEREBELLUM. J. García Ramos. Dept. of Physiology, Res. Ctr. Natl. Polytechnic. Inst, Mexico City, MFXICO.

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Application of square pulses or a.c. currents to the cerebellar surface of the cat gave rise to local potential changes, anodal or cathodal, post-anodal or postcathodal, which occur with a definite latency, may summate in the successive responses, are markedly influenced by polarizing currents and vary with the physiological conditions of the cerebellar cortex.

For these reasons, the potential changes are considered as active responses of the Purkinje cell dendritic membranes. The observations suggest that these membrane potential variations may modulate the excitability for the activation through axodendritic synapses and may constitute the mechanism for the propagation of a potential change through non-synaptic connections between different dendritic branches. The development of positive local responses could be the mechanism of the reduction in excitability which is seen at the locus in the C.N.S. in which the source of an electrical field is created.

INTRA-CELLULAR ANALYSIS OF THE CAT FACIAL NUCLEUS. E. Gardner, T. Tanaka, H. Yu and S. T. Kitai. Morin Memorial Lab., Dept. of Anatomy, Wayne State Univ. Sch. of Med., Detroit, Michigan, U. S. A.

Facial motor neurons (FN) were studied by intra-cellular recording technique in cats anaesthetized with Nembutal. FN were activated by stimulation of the facial nerve (at the periphery and genu), cerebral peduncle (CP), red nucleus (RN), ventral posterior medial nucleus (VPM) of the thalamus, and lateral funiculus (LF) at C-3. During recording, muscular movements were eliminated by gallamine injection and animals were cording, muscular movements were eliminated by gallamine injection to the peak in about 0.5 artificially respirated. Antidromically activated FN spike rose to its peak in about 0.5 msec, had a total duration of around 1 msec and refractoriness of 1.5-2 msec. It was noften succeeded by a period of membrane depolarization (2-6 msec) followed by an after-option of the period of membrane depolarization (2-6 msec) followed by an after-ponents, M, IS and SD spikes. Monosynaptic inputs (indicated by short latency EPSPs) as well as polysynaptic inputs to FN were observed following stimulation of CP, RN and LF. Short latency EPSPs from FN by VPM stimulation also indicated collateral inputs from the trideminal neurons to FN. (Supported by USPHS grants FR 5384-08 and NB 00405-17)

CARDIO-RESPIRATORY FUNCTION IN FREELY SWIMMING PRE- AND POST-SPAWNING PINK SALMON (Oncorhynchus gorbuscha). Walter Garey. Scripps Institution of Oceanography, La Jolla, California, USA.

Studies were conducted at a spawning stream in British Columbia to ascertain steady state values of circulatory and respiratory parameters in pre-spawning fish. Post-spawning fish, undergoing massive degenerative changes and nearing death, were studied for possible alteration of the homeostatic mechanisms. Following an implantation, involving no cutting surgery, of catheters in the dorsal and/or ventral aortas, fish were maintained for days to weeks in the natural ambient conditions of the spawning stream. Among measurements made were the following: Oxygen uptake of the fish, oxygen tensions and contents of arterial and mixed-venous blood, cardiac output, oxygenation of hemoglobin at various oxygen tensions and hydrostatic pressures of blood entering and leaving the gills. A relatively high resting oxygen consumption pertained in pre-spawning fish and persisted undiminished until death. Blood became fully saturated with oxygen at the gill capillaries and the oxygen dissociation curves of blood from pre- and post-spawning fish were nearly identical. The central blood pressures supplying the gills and the periphery remained essentially unchanged from the time the salmon entered the spawning stream until their death. It is concluded that under conditions of a high metabolic activity, spawning, widespread degeneration where many systems are failing, and impending death, the cardio-respiratory relationships are maintained remarkably in pink salmon.

576 ONTOGENY OF THE MYOCARDIAL MEMBRANE PERMEABILITIES. Y.M.Gargoutl and Cl. Bernard. Lab. de Physiologie Animale, ERA-CNRS N°111, 86, Poitiers, France.

Transmembrane action potentials of the rat heart ventricle during ontogeny from the first beats, 9-10 days post-coîtum to the birth, 21 days, have different shapes. Selective inhibitors were used: tetrodotoxin (TTX), an inhibitor of the rapid initial Na+ permeability; manganese chloride (Mn), inhibitor of the "slow Ca++ channel" and tetraethylammonium (TEA), inhibitor of the delayed K+ permeability. At 10 days the heart of rat embryo is TTX insensitive, Mn sensitive and TEA sensitive; at 13 days it is TTX sensitive, Mn sensitive, TEA not at all or slightly sensitive and at 21 days it is TTX, Mn and TEA sensitive. The current-voltage relation in Na+-Ca++-free choline is S-shaped at 21 days but at 13 days there is neither anomalous nor delayed rectification. It seems that: 1) at 10 days, only the slow channel exists, which carries Ca++ ions; it is responsible of contraction; 2) at 13 days, the initial Na+-phase appears, it is implicated in conduction and there is no delayed K+ rectification; 3) at 21 days, the initial rapid phase and the "slow channel" are completed by a delayed K+ permeability, responsible together with the "slow channel" for the response duration. The rat embryo seems a good material to approach the study of permeabilities mechanisms and their molecular supports.

MEMBRANE PHOSPHATASE AND ACTIVE TRANSPORT P J Garrahan and A F Rega, Dept de Química Biologica, Fac de Farmacia y Bioquímica, Univ. de Buenos Aires, Argentina.

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The effect of p-nitrophenylphosphate (p-NPP), a penetrating substrate of the cell membrane potassium-activated phosphatase, on sodium and rubidium fluxes in human red cells was studied. Addition of up to 70 mM p-NPP to the incubation media of ATP-free cells increased both the sodium and rubidium fluxes but the increase was not prevented by 10^{-3} M ouabain, suggesting that the hydrolysis of p²NPP is unable to energize active transport. When added to ATP-containing cells, p-NPP inhibited both ouabain-sensitive sodium efflux and ouabain-sensitive rub idium influx. Inhibition by p-NPP was excerted at the inner surface of the cell membrane with an apparent affinity simmilar to that of the membrane phosphatase and its magnitude was inversely related to the intracellular ATP level. The effects of p-NPP were not due to accumulation of nitrophenol or inorganic phosphate. These results are consistent with the idea that the membrane phosphatase is a part of the system responsible of the active transport of cations. (Supported by the Consejo Nacional de Investigaciones Científicas y Técnicas, Argentina).

CENTRAL NEUROCHEMICAL MECHANISMS OF FOOD MOTIVATION FORMATION IN PIGEONS. G.G. Gasanov. Inst. of Physiology, Azerbaijan Academy of Sciences, Baku, USSR.

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The conservation of excitation state in the lateral part of hypothalamus, hippocampus and motion activity in hungry pigeons with bilateral destruction of midbrain reticular formation is apparently provided not only by nervous mechanisms but by humoral blood factors activating hypothalamus as well. The increase of excitation state in the above-mentioned formations and "hungry" motions of pigeons after medium hypothalamus bilateral destruction assumes that the hypothalamus medium part is one of the decisive links in search excitation system and plays the role of one of the motive food behavioural centres. Bilateral destruction of hippocampus has shown that this brain structure apparently impedes medium structures of hypothalamus and thus by impeding its lateral structures increases the hunger state in pigeons. The analysis of amysyl and chlorpromazine intravenous and intracerebral injections has shown that behavioural food procurating reactions as well as the ascending EEG activation is formed by different neurochemical systems depending on starvation periods.

GONADOTROPIC-LIKE MILK FACTOR. G. H. Gass, Ph.D., M. J. Kolich, M.S. Physiology Dept., Southern Illinois Univ., Carbondale, Illinois, U.S.A.

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The action and identification of an unknown gonadotropic-like milk factor first isolated by K. Vogt, H. Karg, and G. H. Gass at the Institut für Physiologie, Technische Hochschule, München, was investigated. This factor was isolated in the lipid portion of cows' milk (butter fat), and when fed to mice produced an increase in size of the uteri or seminal vesicles of intact weanling mice. This increase in seminal vesicle or uterine weight is proportional to the amount of milk factor incorporated into the mouse diet, and that the resulting increase in uterine or seminal vesicle weight is not the result of increased caloric content of the diet due to the added butter fat was determined by decreasing the non-lipid food consumption by the caloric equivalent of the lipid incorporated in the diet. That the factor is not an estrogen and/or androgen has been demonstrated by using spayed/castrated animals which show no response to the factor as regards uterine weight or seminal vesicle weight. It was also shown that the response to this factor was highest when the butter fat content of the diet was equivalent to a diet containing 60-80% whole dried milk and that higher or lower butter fat containing diets did not produce significant target organ weight changes. The observed changes in target organ weight was observed also in rats and is more pronounced in older weanling animals (23-25 days) than in younger animals (18-22 days), indicating that the response is not peculiar to a single animal species and requires a degree of maturity of the endocrine system, probably the pituitary primarily.

RELATIONSHIP BETWEEN THE INFLUENCES AFFECTING GASTRIC SECRETION AND GASTRIC MUCOSAL CARBOANHYDRASE ACTIVITY ELICITED BY VARIOUS FACTORS IN THE RAT. T.Gáti, P.Keszler, J.Pucsok, L.Szollár, T.Zelles. Pathophysiological Inst., Semmelweis Medical University, Budapest, Hungary. 580

Vibration was found to decrease gastric acid secretion and concomitantly also gastric mucosal carboanhydrase activity in the Shay rat. Gastric mucosa in the Shay rat is known to secrete hydrochloric acid at a maximum rate. In these animals also carboanhydrase activity is higher. In contrast to this linear relationship, Pentagastrin /Peptavlon ICI/ does not change carboanhydrase activity though its secretagogue action is widely recognized. Enzyme activity is likewise not changed by duodenally administered hypertonic sodium chloride solution which inhibits gastric secretion to an extent that the castric content might become even secretion to an extent that pH of the gastric content might become even alkaline.

RELATIONS BETWEEN CIRCADIAN RYTHMS OF THE URINARY CATECHOLAMINES AND TEMPE-RATURE OSCILLATIONS AT THE DIGITAL PADS IN MAN, AS A CONTRIBUTION TO INVESTIGATIONS ON THE ADRENERGIC SYNAPTIC TRANSMISSION. M. GAUTHERIE. Labo. 581

Electroradiology, C.H.U. Strasbourg, France.

The influence of ambient temperature on the circadian rythms of the urinary noradrenaline and adrenaline and of the mean frequency of the skin temperature oscillations at the digital pads has been investigated on eight synchronized healthy adult subjects. The following techniques have been used: fluorimetric assay of the catecholamines, infrared thermometric recording of skin temperatures and statistical electronic computation of the data. On a neuroendocrinological point of view, the main result of this study is related to the fact that the average level, the amplitude and the acrophase of the rythm of the mean frequency of the temperature oscillations and of the rythms of noradrenaline and adrenaline are varying versus the ambient temperature following a similar way. Taking into account the fact already demonstrated by the author that the skin temperature oscillations are centrally commanded by periodical variations of the orthosympa-thetic vasocontrictor tone, the above result brings about an argument in favour of the yet controverted theory according to which the adrenergic synaptic transmission gives rise to a release of both noradrenaline from the nerve terminals and adrenaline from the cutaneous chromaffine cells.

A RAPID FLOW METHOD TO STUDY THE SURFACE PERMEABILITY OF FROG SKIN. U.Gebhardt, W.Fuchs, and B.Lindemann. 2nd Department of Physiology, 665 Homburg, W-Germany.

When the time during which the outer surface of frog skin epithelium is exposed to a test solution is limited to less than 1 s, changes in cellular concentrations are probably negligible and all electrical responses observed during this period will be due to reactions of the outermost resistive membrane of the skin. For such experiments, a rapid flow chamber was developed, which can exchange the bulk solution at the outside of 1 cm2 mem-

brane area within 2 ms by a laminar flow of 50 ml/s.

When replacing Na- by K-gluconate in the outside solution, the time course of the P.D. change can be used to calculate the nominal thickness $\boldsymbol{\delta}_n$ of the unstirred layer reaching down from the outer solution to the first membrane which responds to concentration changes with a change in resting potential. At flow rates of 50 ml/s, a Ringer-agar surface had an unstirred layer with a nominal thickness of δ n= 5 μ , while the outer surface of skin epithelia from Rana esculenta gave values between 5 and 15 μ . They could not be reduced further by increasing the rate of flow. The larger δ values were only slightly lowered after surface foldings had been even ed out by mounting the skin in a state of extreme stretch. The scatter in δ_n values might be due to the epithelia being in different stages of their moulting cycle. However, after inducing an in vitro moult with Aldosteron and peeling off the str. corneum, δ_n was so far not found smaller than before shedding. (This excludes the possibility that a mucous layer at the surface of the skin is responsible for large \mathcal{J}_{n} values.) (Supported by the Deutsche Forschungsgemeinschaft, SFB 38)

WHAT IS PRIMARY IN ACUTE INFLAMMATION: BRADYKININ, HISTAMINE OR 5-HT? A.Gecse, E.Zsilinszky, J. Lonovics. Institute of Pathophysiology, University Medical School of Szeged, Szeged, Hungary.

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The acute inflammation was induced in one of the hind paw of rats of R-Amsterdam strain by the subplantar injection of histamine or 5-HT or dextran.Oedema formation was found 30 minutes after the administration of vasoactive substances.At that time the amount of plasma proteins significantly decreased and the haematocrit increased.Each plasma protein component appeared in the oedema fluid.The prealbumin content has been found to be significantly higher in the oedema than in the plasma.The amount of plasma kininogen /mainly HEMV, plasma bradykininogenase and the esterase activity of the plasma decreased, while the plasma kininase /I and II/ remaind unchanged.Large amount of active kininogenase and kininase was found in the oedema.At the same time esterolytic and proteolytic action was observed in the paw oedema.SBTI or Trasylol partly inhibited the esterase and protease activity. There was no free histamine or 5-HT in the injection site a few minutes after the application of vasoactive amines.C-phenylglycine-n-heptyl ester a bradykinin antagonist significantly reduced the oedema formation.On the basis of our results it seems probable that the histamine and 5-HT are only the triggers in the reaction elicited by them.The bradykinin is important in the amines induced oedema.

NEW DATA ON LOCALIZATION OF CORTICAL CENTER OF PAIN. D.M.Gedevani, G.L. Vepkhvadze, V.A. Mechitashvili. Lab. of Physiology, Med. Inst., Tbilisi, USSR.

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A possibility of evoking an affective behavior of defense-attack (aggressive reaction accompanied by vocalization) by means of an electric excitation of the cerebral cortex was established in cats and dogs. The region of the cortex responsible for this behaviour is on the convex - on the joint of occipital, temporal and parietal regions of the hemisphere. Since such behaviour is similar to the animal response to peripheral pain stimulus, one may think that the experienced pain accompanied by vocalization arises with the participation of the mentioned region of neocortex ("cortical center of pain"). Strong and rather slow biopotentials appear in this region as a response to a peripheral pain stimulus. Such potentials are absent in the case of preliminary injected analgesics. Experiments with a strong electric excitation of a cat's tooth have shown that it suffices to destroy the described cortex region only on one of the hemispheresto remove the pain reaction accompanied by screams. A long electric excitation of the described region causes general epileptic convulsions following the defense-attack reaction.

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GLUCOSE METABOLISM OF SATIETY CENTER IN TISSUE CULTURE: EFFECT OF GOLDTHIO-GLUCOSE. H. M. Geller, R. L. Cechner, D.G. Fleming. Dept. of Biomedical Engineering, Case Western Reserve University, Cleveland, Ohio, USA.

Flying-coverslip roller-tube tissue cultures of mouse hypothalamus were maintained for periods up to six weeks. Glucose uptake and lactic acid production were measured weekly over this period of time. Half of the cultures were incubated with goldthioglucose (GTG) (1 mg/g of tissue). Cultures of ventromedial nucleus (VMN) incubated with GTG showed a significant suppression of glucose uptake compared with either untreated VMN cultures or cultures of the remainder of the hypothalamus. GTG-treated cultures shifted to a more anaerobic form of metabolism, as indicated by an increase in the molar ratio of lactic acid production to glucose uptake. This is interpreted as indicating the presence of glucoreceptor cells in culture.

Supported by a grant from the Cleveland Diabetes Association, an N.I.H. Training Grant (H.G.), and N.I.H. Grant NB-07783 (R.C., D.G.F.).

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DORSAL FRONTAL LOBE AND MOTIVATION. M. Gerbner. Inst. of Psychology, Hung. 586

Academy of Sciences, Budapest, Hungary.

Perseveration is usually considered characteristic for prefrontal lesions and changes of affectivity for medio-basal lesions. Activity of the premotor cortex is generally thought to belong to the motor system. In the present experiments dogs were taught instrumental conditioned and discrimination responses. In other animals repetitive and alternate chains of beination responses. In other animals repetitive and alternate chains of behavioural patterns were trained. Discriminative reactivity and the activation of elements of serial behavioural patterns were affected by dorsal prefrontal injuries in a similar manner as by fasting, and by a lateral premotor lesion in a similar manner as by satiation. In connexion with the lesions affective - motivational behavioural patterns were not observed.

Thus, 1/ dorsal prefrontal and lateral premotor areas are likely to be parts of an interactive control mechanism; 2/ this mechanism may belong to the metivation avater: and 3/ it has were probably a function different the motivation system; and 3/ it has very probably a function different from the limbic and frontal medio-basal structures since it is not associated with affective - motivational behavioural patterns. It may be related with the function which motivates learned reactivity.

DYNAMICS OF TRANSMITTER-RECEPTOR INTERACTION IN VASCULAR SMOOTH MUSCLE. J.Gero, M.Gerová, Inst. of Norm. and Pathol. Physiol. Slovak Academy of Sciences, Bratislava, Czechoslovakia.

Although the amount of transmitter released per stimulus is suggested to be constant the effect of trains of stimuli according to the suggested.

to be constant, the effect of trains of stimuli, equal in number but differing in frequency, as we reported earlier, differ up to 4.3 times.

Supposing that, irrespective of the stimulation pattern, equal contraction should reflect a similar instantaneous receptor occupancy, the events immediately proceeding and exceeding a particular recent occupancy. immediately preceeding and succeeding a particular receptor occupancy, should be similar.

On anesthetized dogs the lumbar sympathetic trunc was stimulated homo-raterally (IG3 - IG4), supramax. amplitude, rectangular impulses, 5 msec. randomized frequency (0,25 - 100 cps) applied in trains, the number of impulses standardized. The diameter and intravascular pressure of the fe-

moral artery and/or vein were registered.

No correlation of the peak value of contraction (i.e. maximal receptor occupation) to the slope of either contraction (rate of transmitter-receptor-assocciation), or relaxation (rate of transmitter-receptor-disceptor-assocciation), or r sociation) was established.

Consequently, some further mechanisms determining the stimulation-vascular response ratio are involved.

SYMPATHETIC CONTROL OF THE AORTA AND MAIN ARTERIES IN RELATION TO THEIR MONOAMINERGIC INNERVATION. M.Gerová, J.Gero, S.Doležel, Inst. of Norm. Pathol. Physiology, Slovak Academy of Sciences, Bratislava, Czechoslovakia. 588

The density of the sympathetic innervation of the aorta, carotid and femoral arteries in dogs was correlated with the range of sympathetic confemoral arteries in dogs was correlated with the range of sympathetic curtrol. Using the Falck-Hillarp method the following gradation in density of the monoaminergic innervation was established: femoral artery-carotid artery-aorta. In the femoral artery the very few terminals are dispersed in the adventitia only, whereas in the carotid artery and aorta the nerve fibres are distributed in the outer layers of the media.

The vessel diameter monitored in vivo at constant pressure, the sympathetic trunc was stimulated at the respective level. The maximal decrease in diameter in relation to resting value ellicited by supramaximal sti-

thetic trunc was stimulated at the respective level. The maximal decrease in diameter in relation to resting value ellicited by supramaximal stimulation was as follows: Aorta, above the iliac bifurcation: 5,5 ± 0,1 %. The range of contraction was fainting cranially: below the renal arteries it represented only 2,2 ± 0,2 %. Maximal constriction of the carotid artery was 3,3 ± 0,4 %. In spite of the very poor sympathetic innervation the maximal contraction of the femoral artery was as high as 13,42+1,2 %.

It is concluded that no correlation between the density of sympathetic terminals and the effective constriction of main arteries exists.

IDENTICAL PROPERTIES OF ACETYLCHOLINE AND 5-HYDROXYTRYPTAMINE-C-RECEPTORS IN A SINGLE SNAIL NEURON. H.M. Gerschenfeld, Laboratoire de Neurophysiologie Cellulaire, CNRS, 4 av. Gordon Bennett, Paris, France.

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5-Hydroxytryptamine (5-HT) may cause three different effects on single snail neurons:
1) a mainly Na⁺ dependent excitation, 2) a K⁺ dependent inhibition, or 3) a Cl⁻ dependent inhibition. The 5-HT receptors involved in these actions, conventionally called A, B and C receptors respectively, are pharmacologically different among them (Science, 1971, in press). The present experiments deal with the pharmacological similarity between 5-HT-C-receptors and acetylcholine (ACh) receptors present on the same neuron. Activation of both types of receptors is associated with increase in Cl⁻ permeability. Moreover, both types of receptors may be blocked by the same low concentrations (10-5 M) of cholinergic antagonists (d-tubocurarine, atropine), anticholinesterase drugs (prostigmine, edrophonium), 5-HT antagonists (LSD 25, tryptamine) and monoamine oxidase inhibitors (iproniazide, isocarboxazide). Crossed desentization between ACh and 5-HT is observed in neurons endowed with 5-HT-C-receptors, either by combining ionophoretic applications of both substances or perfusing very low concentrations of one of them while applying the other iontophoretically. The possible mechanisms of this identity between receptors to ACh and 5-HT will be discussed.

RESPONSES OF AUDITORY NEURONS OF THE INFERIOR COLLICULUS TO AMPLITUDE-MODULATED SOUNDS. G.V.Gersuni, I.A.Vartanian. Pavlov Inst.of Physiology, Academy of Sciences, Leningrad, USSR.

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Responses of 208 neurons of the inferior colliculus of white rats were studied. Amplitude-modulated sounds with low modulation rates (1-100 Hz) and high carrier frequency (1.5-24 kHz) were used. The following data were obtained. 1. An increase in the difference between the carrier frequency of the signal and the characteristic frequency of the neuron leads to: (a) diminution of the reproduced modulation rate in the discharge of the neuron up to a complete inhibition of the discharge; (b) a shift of the discharge of the neuron relative to the phase of the modulation cycle of the signal. 2. Appearance of long lasting after-discharges which reproduced important features of the signal (modulation rate, phase relations) in specific conditions of stimulation (combination of definite values of amplitude-modulation rate, carrier frequency and intensity level). It can be assumed that when stimulated with different amplitude-modulated sounds, the specifity of the responses of collicular neurons is created by excitatory-inhibitory inputs interrelation.

MULTIPLE COLLATERAL PATHWAYS IN HIPPOCAMPUS. T. Gessi*, N.Y.U. Med. School and P.H.R.I., N.Y.C., USA.

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The predominant axon collateral action in hippocampus is known to be a recurrent, powerful long-lasting inhibition, the basket cells being identified as the inhibitory interneuron. The present work on cat hippocampus extends this conception in several ways. Upon stimulation of the deafferented fornix: 1) IPSPs were recorded intracellularly in the CA4 region, an area described as devoid of the basket cell plexus; 2) a pause in extracellular unit discharges in the granule cell layer of the dentate gyrus was observed; 3) a slow field potential with time-course parallel to the later phase of the recurrent IPSPs in CA1 to CA3 has been identified: it is not associated with any "idle cell" transmembrane potential and has a superficial positive - deep negative depth configuration; 4) short-latency recurrent EPSPs and a superficial negative field potential were recorded. These data reveal the existence of multiple collateral actions by the pyramidal cell axons of the fornix.

(Supported by USPHS Grant NB05980 and NS09361). *N.A.T.O. Fellow.

ADRENERGIC MECHANISM IN PORTAL VEIN. A.M.Geumei, F.A.Bashour, S.J.Kechejian. Cardio-pulmonary Institute, Methodist Hospital, University of Texas, Dallas, Texas, USA.

Direct effects of adrenergic stimulants and blockers on portal vein were investigated in intact anesthetized dog. Portal vein flow (PVF) was measured using electromagnetic flowmeter. Mean systemic arterial (FA), portal venous (PV), hepatic wedge (NW) and vein pressures were measured simultaneously. Portal vein resistance (PVR) was calculated before and for 5 min. after intraportal administration of Norepinephrine (NE, 10), Epinephrine (Epi, 10), Isoproternol (ISp, 10) in normal dogs (n=31) and after pre-treatment with Phenoxybenzamine (PNB, 1 mg/kg) (n=18) and Propranolol (PRP, 1 mg/kg) (n=15).

(n=15).
Immediate effects (within 15 sec.) of adrenergic agents on PVR are summarized in

able and re	eported as percent of c	PNB	PRP
	Normal	150 (12)	157 (11)
NE	161 (16) 169 (22)	146 (15)	185 (16)
Epi Isp	101 (0.7)	102 (1.1)	114 (5) SEM=()
Tab			

In conclusion, endogenous catecholamines (NE, Epi) constrict the portal vein, while isoproternol has an insignificant effect.

CYSTEINE AND PCF, IN BRAIN METABOLIC DESEQUILIBRIUM DETERMINED BY IONIZ-ING RADIATIONS. 9 N.Gheorghe. Inst. of Normal and Pathol. Physiology, Bucharest, Romania.

In the present paper it is shown that the x and gamma ionizing radiations and rapid neutrons in 750 r and 1000 rad doses produce in the brain a series of molecular lesions. These lesions are related to modifications in the structure and composition of nucleic acids, hydrosoluble proteins, aminoacids, purinic and pyrimidinic bases, cetoacids, estherified and non-estherified free fatty acids, non-saturated fatty acids, phospholipids and other lipidic fractions. We believe that the protection of macromolecules, which have a major biological importance, against the injurious effects of physical agents is related to the possibility of reconstructing the molecular alterations, in view of reestablishing the normal vital processes. For that purpose the effect of cysteine upon the reestablishment of the metabolic desequilibrium induced in brain by ionizing radiations was followed in comparison with that of the PCF product, before and after irradiation. It is shown that the action of cysteine and PCF product in reestablishing the cerebral metabolic desequilibrium in irradiated animals is only partial.

594 INFLUENCE OF THYROID UPON GLYCOLIPIDS IN DEVELOPING CEREBRAL CORTEX AND CEREBELLUM OF THE RAT. N.E.Ghittoni and I.F.de Raveglia. Dept.Biol. Chemistry, Sch.Pharmacy and Biochemistry, Univ.Buenos Aires, ARGENTINA

The lack of thyroid function from birth produces profound alterations in the histological and biochemical differentiation of the nervous system. This report describes the effect of neonatal radiothyroidectomy upon cholesterol and glycolipids from cerebral cortex and cerebellum of growing rats. Although 5 and 10 days cretin rats did not show any differences with normal controls, a significative decrease in cholesterol, cerebrosides, and also in the four major gangliosides, was found in cerebral cortex from 20 and 30 days thyroidectomized rats. This impairment in the concentration of gangliosides from cerebral cortex is consistent with the marked hypoplasia of both the axonal and dendritic components of the cortical neuropil from thyroid deficient rats. Cerebellar glycolipids were only partially affected by neonatal thyroidectomy, pressumably because of the ontogenetical heterogeneousness of the cerebellum.

THE ENERGETICS OF RAT SOLEUS MUSCLE. C.L.Gibbs, Dept.of Physiology, Monash University, Melbourne, Victoria, Australia.

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Up until the present time most myothermic investigations into the energetics of contraction have been carried out using amphibian skeletal muscle. The aim of the present experiments was to adapt the myothermic technique to allow investigation of a mammalian muscle preparation. Rat soleus muscles were chosen and both the initial and recovery energy production were measured. Tetanic isometric and isotonic contractions were examined at $27^{\circ}\mathrm{C}$, the muscles being stimulated for 2 seconds at $30/\mathrm{sec}$. The total energy production was maximal with loads between 0.5 and 0.8 P_{o} and was minimal when the lightest loads (< 0.1 P_{o}) were being lifted. In 10 experiments the maximum ratio at work/(work + total heat) ranged between 0.13 and 0.29 and the maximum isometric heat rate/g.muscle between 79 and 2^{41} g.cm./(g.sec). The isometric heat rate declined at lengths above and below 1_{o} . Results obtained suggest that although there are many similarities between the energy production of mammalian skeletal muscle at $27^{\circ}\mathrm{C}$ and of amphibian muscle at low temperatures there are also significant differences. In particular present results indicate that the mechanical efficiency of this muscle under optimum conditions will be high in comparison to frog sartorius muscle.

MFASUREMENT OF K-42 FLUXES ACROSS SINGLE DISTAL TUBULES OF RAT KIDNEYS. G. Giebisch, P.F. curran, M. Mello-Aires and G. Malnic. Depts. of Physiology, Yale Univ. School of Medicine, New Haven, Conn., USA, and Univ. of Sao Paulo Medical School, Sao Paulo, Brazil.

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Unidirectional fluxes of K-42 across the luminal and peritubular cell membranes and the potassium transport pool of superficial distal tubules were measured by (1) perfusing peritubular capillaries with K-42 containing Ringer's solution and observing the steady-state transepithelial potassium influx into the tubular lumen during continuous perfusion of the latter with non-radioactive equilibrium solutions and (2) by subsequently observing washout of K-42 from tubule cells into the lumen after discontinuing peritubular perfusion with K-42. Experiments were carried out in animals on a normal, low and high potassium intake and in bicarbonate-loaded animals. Distal tubular potassium secretion was depressed in low-K animals and stimulated in animals on a high potassium intake and after bicarbonate loading. Transition from low to high distal tubular potassium secretion is initiated: (1) by enhanced peritubular active uptake of potassium and (2) by an increase in the distal tubular potassium transport pool.

LOCALIZATION OF CENTRAL NERVOUS SYSTEM VASOPRESSOR ACTIVITY OF ANGIOTENSIN.

P. L. Gildenberg, C. M. Ferrario, R. J. Alfidi, J. W. McCubbin. Cleveland Clinic Foundation, Cleveland, Ohio, U.S.A.

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The infusion of angiotensin into the vertebral arteries of dogs anesthetized with chloralose at doses which are ineffective intravenously results in an increase in systemic blood pressure. It had previously been reported that, as demonstrated by selective ligation of the basilar or vertebral arteries, the site of this activity is at the level of the lower medulla (Physiologist 12: 235, 1969). This pressor response is mediated by the sympathetic nervous system, since it is abolished by a section of the spinal cord at upper cervical levels or sympathetic blocking agents, but is unaltered even after a midbrain section. The response to low doses of angiotensin in the vertebral arteries can be abolished by coagulation of the area postrema, and can be reversibly diminished by local cooling of that structure. Thus, the area postrema is a responsive site for the central effects of angiotensin, and the pressor activity is mediated via the sympathetic nervous system. (Supported in part by USPHS Grant H-6835, National Heart and Lung Institute).

INCORPORATION OF INORGANIC PHOSPHATE INTO ATP, CATALYSED BY TENSION, IN GLYCERINATED FIBRES. J.M. Gillis and G. Maréchal. Dept de Physiologie, Univ. de Louvain, Louvain, Belgium.

The hypothesis of a reversal of the ATPase activity during stretch of contracted muscle has been checked by stretching glycerinated fibres incubated in the presence of \$32p_i\$, ADP, and ATP. Labelled ATP has been obtained (Gillis & Maréchal, 1969, IIIrd int. Congress Biophys.; confirmed on insect fibres by Mannherz, 1970, FEBS letters 10). In new experiments made in the presence of azide and oligomycin, \$32p_i\$ incorporation into ATP was compared between contractions with stretch or release, and isometric or isotonic (with zero load) contractions. Pi incorporation depends on both the duration of contraction and the tension developed, as demonstrated by a linear relationship between the incorporation and the tension-time integral. No specific effect of the stretch is observed. The increased incorporation in stretched muscle can thus be explained by the high tension produced and cannot be taken as a demonstration of the reversal of the ATPase.

PHARMACODYNAMICS OF MAGNESIUM CETOGLUTARATE. A. Giráldez, N. Mylonakis, E. Mañé. Departamento Investigaciones Farmacológicas, Barcelona, Spain.

The α -cetoglutaric acid has been employed as an energetic drug for its importance in the Krebs cicle and the ion magnesium is considered as a nonspecific catalyst of biochemical reactions and, as such, is used in therapy; therefore we have been studying the pharmacodynamics of the magnesium α -cetoglutarate, salt not used as a medicament still. The absorption of this substance has been studied as well for oral way as for the parenteral one, establishing the levels of magnesium and α -cetoglutaric acid in rabbits and rats blood treated with magnesium α -cetoglutarate comparing them with those obtained with other magnesium salts of therapy use as chloride, sulphate, aspartate, gluconate, glycerophosphate, and ascorbate. The serum levels of magnesium obtained with magnesium α -cetoglutarate present a peack during the first hour, being comparables with those obtained with other magnesium organic salts, the levels of α -cetoglutaric acid also present a peack during the first hour. The intestinal absorption of the different magnesium salts have been investigated with the technics of the absorptions in the same loop of the same animal "in vivo". The biggest or the smallest easiness of transit of this substances through the blood-brain barrier has been related with the partition coefficients obtained in chromatography of hydrophil and Idpophil phases. The characteristics of different magnesium salts are described with regard to the local tolerance, to the irritation of the gastric mucous membrane and to the influence about the speedness of intestinal transit.

SENSITIVITY OF THE EARLY RECEPTOR POTENTIAL TO UREA. L.Giulio and L. Petrosini. Inst. of Physiology of Domestic Animals, Univ. of Perugia, Perugia, Italy.

Incubation of dark-adapted, excised and equatorially dissected frog eyes with 2-4-6-8 M urea in physiological saline, drastically reduces or irreversibly abolishes the early receptor potential. Evidence is presented which indicates that the abolition of the early receptor potential arises simultaneously with a disappearance of the dichroic properties of photoreceptors. It is suggested that the breakdown of some direct electrostatic interactions (e.g.hydrogen bonds) between the pigment molecules responsible for the early receptor potential causes the loss of the orientation of the molecules themselves (which are identifiable, from an electrical point of view, with the current microgenerators). Supported by a grant from the C.N.R. (contratto di ricerca N. 69.02159 115.2291.0).

PREFERENTIAL VULNERABILITY OF THE TRANSCALLOSAL EVOKED RESPONSE (TCR) TO HYPOXIA. C. Giurgea, F. Moyersoons. UCB - DIPHA, DRD, Dept. Pharmacology, Brussels, BELGIUM.

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In curarised cats, cortical EEG, phonocardiogram, electrocardiogram and TCR were recorded. Nitrogen induced hypoxia was gradually produced up to clear—cut EEG-"silence" and autonomic irregularities. When studying recovery after hypoxia, it was found that significant impairement of the TCR was maintained 20-60 minutes after full EEG and autonomic restoration. Preliminary pharmacological investigation shows PIRACETAM to counteract hypoxia-induced events. Discussion is made on the physiological and physiopathological implications of this finding.

STUDIES ON THE HYPOTHALAMIC CONTROL OF SOME VEGETATIVE FUNCTIONS. L. Glavcheva, L. Petrov, V. Velkova. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

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Acute experiments (cats) have been carried out to study the effect of the electrical stimulation of the lateral preoptic region on both the intestinal motor activity and arterial pressure. Activation of the intestinal motility and fall in the blood pressure were the phenomena most frequently observed upon stimulation of this region. This suggests that the lateral preoptic region exerts mainly a parasympathetic effect on the vegetative functions under investigation. It was established that upon stimulation of the lateral preoptic region uniform as well as opposite vegetative states were found in the cardiovascular system and intestine, too. There is evidence to show that the rapid and considerable increase in the blood pressure bears a relation to the increased intestinal activity. The activation of the intestine in these cases is postulated to be a result of increased baroreceptory reflexes.

EFFECTS OF A VERTICAL GRADIENT OF TRANSPULMONARY PRESSURE ON EXCISED LUNG P-V CHARACTERISTICS: D.H. Glaister, J. Milic-Emili, R.C. Schroter, M.F. Sudlow; P.F.S.U. Imperial Col. London, and R.A.F. Inst. Aviat. Med. Farnborough, U.K.

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The pressure volume characteristics of excised canine lungs and lobes were investigated both when suspended in air and when supported in an artificial pleural pressure gradient. The gradient was produced by immersing the preparation in a 'fluidised bed' (Schroter & Sudlow J. Physiol. 200, 3P, '68) consisting of small polystyrene beads which were agitated by a slow upcurrent of air. The beads were 'fluidised' and the bed behaved as if it were a liquid of density 0.25 gm/cc. The lungs were usually ventilated between mean transpulmonary pressures (TPP) of +30 and -5cmH₂O, this produced the same vital capacity both in air and the bed. The shapes of the air and bed P-V curves were similar, but there were significant differences. The bed curves were elongated on the pressure axis and not simply displaced from the air curves by an amount equal to the increased mean pleural pressure. The site of beginning of airway 'closure' on deflation both in air and the bed was positive (approx.+2.5 cmH₂O TPP). The onset of 'opening' was approx. +9.5 cmH₂O TPP. The differing shapes of the air and bed curves resulted from different patterns of sequential opening and closing of lung units caused by the presence of a gradient of transpulmonary pressure in the bed but not in air.

VENTILATED DISTRIBUTION IN EXCISED LUNGS: D.H. Glaister, J. Milic-Emili, R.C. Schroter, M.F. Sudlow: P.F.S.U., Imperial Col. London & RA.F. Inst. Aviat. Med. Farnborough. U.K.

In normal crect man the distribution of ventilation in the lungs is determined by the vertical gradient of transpulmonary pressure (P_{TPP}). We studied the effects of such a gradient of P_{TPP} on the distribution of inspired gas in excised unperfused lungs. Lungs were suspended in air where P_{TP} is uniform and in a fluidised bed - where the P_{TP} gradient is similar to that in vivo. The distribution of gas was studied by injecting boluses of radioactive Xenon, scanning the lungs on inflation and monitoring the subsequent washout of expired gas at the trachea. In air, boluses inspired at low lung volumes were preferentially distributed to the upper parts of dog lungs. The subsequent deflation washout curve showed a gently rising alveolar plateau with a slight terminal rise. With a vertical gradient of P_{TP} there was more preferential distribution of gas to the upper zones and washout curves were irregular with a marked terminal rise. In monkey lungs, in air, the bolus was evenly distributed but the upper zones again received more Xe when the lungs were in the fluidised bed. Washout curves were flat in air but had a terminal rise in the bed. The changes could be predicted from the measured elastic properties and show uneven distribution of gas between lobes and within lobes of lungs. The terminal rises in the alveolar plateaux of the washouts support the hypothesis of airway closure in the most dependent regions of the lungs.

THE EFFECT OF SYNTHETIC ACTH /3 1-28 CORTICOTROPHINE/ ON THE STEROID BIOSYNTHESIS OF RAT ADRENALS. E.Gláz., R.Kiss., M.Péteri., V.Morvai and É.Fodor. 2nd Department of Medicine, University of Budapest, Budapest, Hungary.

As it has already been demonstrated by the authors /Gláz et al., 1969/, two synthetic ACTH preparations with different amino acid sequences /3¹⁻²⁴- and/3¹⁻²⁸- corticotrophine/ have the same stimulating effect on the steroid biosynthesis of rat adrenals in vitro, as regards aldosterone and corticosterone. In the present experiments synthetic/3¹⁻²⁸-corticotrophine/Humacthid, G.Richter, Budapest/ was given to rat adrenals in vitro, the steroid biosynthesis of which had been previously suppressed with DOCA+salt loading on the one hand, and dexamethasone pretreatment on the other hand. Changes in the biosynthesis of aldosterone and corticosterone were recorded with the help of Pregnenolone -16-H3, i.e. by measuring the specific activity of the above mentioned steroids. The results of these experiments demonstrated the characteristic steroid biosynthesis-stimulating effect of this synthetic ACTH preparation not only under basic conditions but also in cases when the adrenal steroid biosynthesis has been suppressed by various means, i.e. the aldosterone by DOCA+salt loading and by dexamethasone, and the corticosterone by dexamethasone pretreatment.

ASSESSMENT OF THE RELATIVE ROLES OF VARIOUS LUNG REFLEXES BY BILATERAL ANODAL BLOCK OF VAGAL CONDUCTION. M.Glogowska and J.G. Widdicombe. Polish Academy of Sciences, Warsaw, Poland and University Laboratory of Physiology, Oxford, England.

We have studied the rapid shallow breathing and hyperventilation of anaesthetized cats and rabbits due to (1) pulmonary congestion caused by inflation of a balloon in the left atrium, (2) inhalation of sulphur dioxide gas in air, (3) intravenous injections of histamine and inhalation of its aerosol and (4) intravenous injections of phenyl diguanide. Three types of lung receptor are affected, pulmonary stretch receptors, lung irritant (epithelial) receptors, and alveolar J-receptors. Single fibre recording from the vagus shows that the three types of receptor are influenced by the procedures, but primary respiratory responses come from the irritant and J-receptors. Bilateral anodal block of the vagus nerves can cause block of conduction in the myelinated A-fibres, while conduction in the non-myelinated C-fibres (from J-receptors) continues. The method has been tested both by recording compound electroneurograms and by single-fibre recording with and without anodal block. Results from both methods indicate that for none of the examples can a single afferent pathway from the lungs be exclusively implicated, but that the relative involvement of the three afferent pathways varies between the lung conditions studied.

The effects of neuroleptics on the reflex excitability in man. F. Glötzner. Max-Planck-Institut für Psychiatrie, 8 München 13, Kraepelinstraße 10.

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The clinical examination of patients treated with neuroleptics seemed to show an enhancement of reflex activity accompanying severe parkinsonoid side-effects. In order to verify this observation, the reflex excitability of schizophrenics was investigated before and during neuroleptic treatment. The degree of reflex excitability was measured by the time-course of the postreflex recovery of the Hoffmann reflex(H-reflex). The N. tibialis was stimulated with two identical electrical stimuli at varying time intervals. Then the amplitudes of both reflex-responses were compared to define the degree of recovery. All patients with parkinsonoid side-effects - estimated clinically by means of a rating scale - showed an earlier and higher and even overshooting recovery of the H-reflex-amplitude as compared with the recovery curves of the same patients before neuroleptic treatment. Simular changes of the recovery cycle were found in Parkinson's disease. It can be assumed, that this more rapid recovery is the consequence of a raised excitability of motoncurones. The possible sites of action of neuroleptic drugs in the extrapyramidal and perhaps pyramidal systems are discussed.

DIGITALIS RECEPTORS IN ISOLATED HEART TISSUE. T. Godfraind and M. Lesne

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Laboratoire de Pharmacodynamie Générale, Univ. de Louvain, Belgium.

Digitalis receptors have been studied in isolated guinea pig atria by monitoring the uptake of tritiated cardiac glycosides in various experimental conditions. Analysis of uptake enabled a non saturable and a saturable binding site to be distinguished. There are several experimental findings supporting the evidence that the saturable binding site is a specific binding site. Equilibrium constants expressed in nmol were equal to 208 for digitoxin and to 312 for ouabain. Alteration of cell metabolism either by reduction of temperature or by metabolic inhibitors modified the binding to the specific site. These findings support the view that the binding of cardiac glycosides to isolated tissues is controlled in a same way that their binding to subcellular fragments with a high specific activity of Na-K-ATPase.

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EFFECTS OF Di-n-PROPYLACETATE (DPA) ON BRAIN GABA AND ENERGY RICH COMPOUNDS; CORRELATIONS WITH PROTECTION AGAINST CONVULSIONS. Y.Godin, J.Mark, S.Simler and H.Randrianarisoa. Centre de Neurochimie du CNRS, Institut de Chimie Biologique, Faculté de Médicine, 67-Strasbourg, France.

DPA increases the mouse brain GABA content by about 50 % while the amounts of other amino acids, and the biosynthesis of GABA from glutamic acid, do not change. DPA inhibits glutamate decarboxylase and, to a higher degree, GABA transaminase activities. This observation might explain the increased GABA level, suggesting a mechanism for the regulation of the amount of this compound in brain. A strong correlation between the increase of brain GABA and anticonvulsive protection against audiogenic seizure could be demonstrated. Simultaneously brain ATP and phosphocreatine content increase. The correlations between the inhibitory effect of GABA, the increase of energy rich compounds, and protection against convulsions will be discussed.

REGULATION OF LIPID METABOLISM IN THE ISOLATED PERFUSED LUNG. Rodolfo I. Godinez and William J. Longmore. Dept. of Biochemistry, St. Louis Univ. Sch. Med., St. Louis, Missouri 63104, USA.

Studies, using an isolated perfused rat lung preparation, have been carried out to determine if variations of glucose concentration of the perfusate alter lung lipid determine if variations of glucose concentration of the perfusate containing 1.5 mM or 5.6 mM glucose and either 4 mM acetate or 0.5 mM palmitate. Lung lipids were extracted and separated by silicic acid column chromatography. A 37% increase in phospholipid phosphorus content was observed in lungs perfused with 1.5 mM glucose as compared to lungs perfused with 5.6 mM glucose, independent of the presence of either acetate or palmitate. A similar increase in the incorporation of acetate-1-14C and palmitate-1-14C into phospholipid was observed. The phospholipids were then chromatographed on silicic acid by a discontinuous gradient. An increase of 42% in the second component eluted with CHCL₂:CH₃OH:H₂O (5:1:1%) was observed in lungs perfused with 1.5 mM glucose as compared to lungs perfused with 5.6 mM glucose. Preliminary results of the purification of this fraction by TLC followed by analysis of the fatty acids (by GLC) of the lecithin thus obtained have shown no alteration in the composition of this fraction with change in glucose concentration. These findings suggest that circulating glucose concentration may be a regulatory factor in lung phospholipid metabolism. (Supported in part by USPHS HE-13405, HE-5672 and Missouri Heart Assoc.)

DISTRIBUTION OF CATECHOLAMINES ALONG THE DIGESTIVE TRACT. M. Goffart. Dept. of Physiology, University of Liège, Belgium.

The noradrenaline (NA) and adrenaline (A) contents of the wall of the digestive tract have been estimated by the method of EULER and FLODING in cat, dog, guinea-pig and rabbit. The total amount of NA + A ranges between 0.05 and 0.9 µg/g fresh tissue. The pattern of distribution of catecholamine contents along the digestive tract is different in each species. These gradients will be compared with those of A.Ch, 5-HT, histamine and substance P. The relative amount of A does not exceed an average of 4 per cent. It seems that A is, at least in part, located in chromaffine tissue as its average percentage increases up to 17 per cent after denervation. Catecholamines are unequally distributed in the mucosa plus submucosa and in the muscular coat of the same segment.

612 PROPERTIES OF INSECT U.V.-RECEPTORS. M. Gogala, P. Stušek. Inst. of Biology and Biol. Dept. of Biotechnical Faculty, Univ. Ljubljana, Yugoslavia

A specific feature of arthropode receptors is their high sensitivity to u.v. rays. The compound eye of Ascalaphus macaronius Scop. and the ocelli of Oncopeltus fasciatus Dall. represent specialized receptor organs suitable for studying u.v. reception. Spectral sensitivity, the adaptation course and the relation of potential amplitudes to the intensity of stimuli, were electrophysiologically determined. U.v. receptors with maximum sensitivity at 340 nm and, additionally, "green" receptors, the later only in "lateral eyes" of A. m. and in ocelli of O. f., were found. There is good agreement among electrophysiological data, ethological observations and the properties of the u.v. visual pigment recently isolated from the eyes of Ascalaphus.

CIGARETTE SMOKING AND EXERCISE. $\underline{\text{A.N. Goldbarg}}$, $\underline{\text{R.J. Krone}}$, and $\underline{\text{L. Resnekov}}$. Dept. of Medicine, University of Chicago, Chicago, Ill. U.S.A.

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The circulatory response to upright bicycle exercise was investigated in 9 healthy male smokers before and after smoking a single "reference" cigarette. Catheters were positioned in the pulmonary artery (PA) and a systemic artery. Expired air was collected for gas analysis. Cardiac output (Q) was determined with the Fick principle.

Smoking increased \dot{Q} 20% at rest (p \dot{Q} .05), % at 300 kpm/min, but was unchanged at higher levels of exercise. Since heart rate increased significantly about 20 beats per minute at rest and at all levels of exercise, stroke volume remained unchanged at rest and decreased % (p \dot{Q} .001) at the highest level of exercise. \dot{V} 02, arteriovenous 02 difference, PA pressure and calculated systemic peripheral vascular resistance were unchanged after smoking.

These results, which are at variance with previous reports of increased stroke volume during supine exercise, cast doubt on the usual assumption that the cardio-vascular effects of cigarette smoking are due entirely to catecholamine release by nicotine. Either a direct negative inotropic effect or a decrease in peripheral venous return at high levels of exercise must be involved to explain our findings.

CHANGING THE BEHAVIORAL SIGNIFICANCE OF A VISUAL STIMULUS AFFECTS THE RESPONSE OF NEURONS IN MONKEY SUPERIOR COLLICULUS. Michael E. Goldberg and Robert H. Wurtz, Lab of Neurobiology, Natl. Inst. of Mental Health, Bethesda, Md., U.S.A.

Rhesus monkeys were trained to fixate a stationary spot of light on a screen for several seconds to obtain a reward. The receptive fields of single units in the superficial gray and optic layers were then determined with a second spot of light (RF spot) while the monkey continued to look at the fixation point. Small (10 x 10) stationary spots were effective in activating most units with a latency of less than 50 msec. The response of a unit to a RF spot coming on at one point in the receptive field was studied. Then, this RF spot was made more significant for the monkey: the fixation point was turned off at the same time the RF spot was turned on and the monkey made a saccade to the RF spot as he had been trained to do, instead of ignoring it as before. In the 200-300 msec between the onset of the RF spot and the saccade, the RF spot fell on the previously studied place in the unit's RF. In this case, however, the unit responded to the stimulus onset with a more regular and vigorous discharge. This enhancement of response was frequently clearer in the first few trials after the RF spot became the saccade target, and was usually sharper when the RF spot was near the edge of the RF. The enhancement was not observed for all units and was occasionally detectable when a saccade was made to a point outside the RF. These findings indicate that not only the physical properties of a stimulus, but also its behavioral significance determines the response of certain superior colliculus units.

EFFECT OF INHIBITORS AND CONCENTRATION GRADIENTS ON SUGAR TRANSPORT IN RABBIT ILEUM.

A. M. Goldner, and P. F. Curran. Department of Human Physiology, Univ. of California, Med. School, Davis, California and Department of Physiology, Yale Univ. Medical School, New Haven, Connecticut.

The unidirectional influx of sugar across the brush border of the intestinal epithelium and the transfer across the entire intestinal epithelium are both dependent on sodium in the mucosal bathing medium. A l:l relation exists between sugar and Na influx suggesting that there is a coupled entry of Na and sugar into the cells. The presence of cyanide $(2\times10^{-3}\text{M})$, dinitrophenol (10^{-4}M) , ouabain (10^{-4}M) and monoiodoacetate (10^{-3}M) in the bathing medium virtually abolished the net transport of sugar across the intestine. Under the same conditions the sodium dependent sugar influx was minimally effected. Furthermore, mucosal strips treated with ouabain (10^{-4}M) to elevate intracellular Na extruded sugar against a concentration gradient when cell Na concentration exceeded the Na concentration in the bathing medium. Similarly Na extrusion occurred against a concentration gradient when intracellular sugar exceeded extracellular sugar concentration. These results indicate: 1) the inhibition of transmural transport or accummulation by these inhibitors was not caused by an impairment of the influx process; 2) the influx of sugar is not tightly coupled to metabolic energy; 3) the movement of Na down its concentration gradient is able to transport sugar against its concentration gradient. These results support the hypothesis that the Na gradient between the intracellular and extracellular environment is a sufficient driving force for the transport of sugar. (Supported by a grant from U.S.P.H.S.).

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616 THE DRINKING OF LABORATORY DOGS WHICH ACCOMPANIES CHANGES IN FOOD INTAKE. P. Golob, W.J. O'Connor and D.J. Potts. Department of Physiology, University of Leeds, Leeds, Britain.

Laboratory dogs, kept in metabolism cages for periods of 26 - 36 consecutive days with drinking water continuously available were fed a mixture of either proprietary dog biscuit and raw beef or of suet, raw beef and a biscuit of low protein content, at 17.00 each day. Drinking, monitored by a continuously recording meter, occurred during times of activity and raised evaporative loss during the daytime before 17.00 (O'Connor and Potts, 1969) and also, to a smaller degree, after feeding as was particularly described by Gregerson (1932). When the dogs were allowed a double ration of either diet the 24 hour water intake increased, due to increased drinking after feeding. At the end of the overfeeding period this drinking promptly returned to the control level. When the effects of extra fat, carbohydrate and protein were separately investigated, increased water intake occurred after additional quantities of carbohydrate and protein, but not fat, had been added to the daily food ration. The drinking which occurred at other times of the day was not affected by these changes in diet. References: O'Connor, W. J. and Potts, D. J. (1969). Quart. J. exp. Physiol., 54, 244-265. Gregerson, M. I. (1932). Amer. J. Physiol., 102, 344-349.

RELATIONSHIP BETWEEN SOME STEROIDS AND THE ELECTRICAL ACTIVITY OF THE CENTRAL NERVOUS SYSTEM OF THE RAT. R.Gómez.; M.A.Requena.; E.Vallecalle. Dept. Physiology, Vargas Med.Sch., U.C. V., Caracas, Venezuela.

Adult Sprague-Dawley rats of both sexes have been submitted to different treatments:Bilateral adrenalectomy, administration of DOCA (1 miligr.daily) and hidrocortisone (1 miligr.daily), castration, administration of progesterone and estradiol (5 microgr.daily). In all these rats we studied the spontaneous electrical activity (ECoC) of the central nervous system under anesthesia or curarizing drugs and the averaged evoked potential in the sensorimotor areas. Adrenalectomy, castration, Progesterone and Testoterone increase the sensibility to barbiturate while estradiol increases the amplitude of evoked potential and the resistance to barbiturate anesthesia. DOCA and Cortisone increase the resistance to barbiturate in normal and adrenalectomized animals. The local aplication to the cortex of conjugated oestrogenic substance origines a focus of hiperexcitability similar to the one developed by Peniciline or cobalt whith increase of the amplitude of the evoked potential. The spikes and afterdischarges of this focus are cleared by Cloridediazepoxide.

FURTHER STUDIES ON THE ULTRASTRUCTURE OF THE MOUSE ADENOHYPOPHYSIS.

C.L.A.Gómez-Dumm and J.M.Echave-Llanos. Inst.Embriol.Biol.Histol., Fac.de
Ciencias Médicas, Universidad Nacional de La Plata, La Plata, Argentina.

The fine structure of the pars distalis of young and adult male mice was studied. Most of the granular parenchymal cells did not show remarkable differences comparing with previous observations. As the follicular cells were seen very seldom, it is difficult to assume that they are the source of ACTH in the mouse. On the other hand, numerous large irregular cells with many small cytoplasmic vesicles were found. They are believed to be corticotrophs by others. A peculiar cell type was seen near the blood vessels. The cytoplasm contains vesicles measuring more than 350 mp in diameter. They seem to be spilling their content, which is of low electron-density, in the cell matrix. This finding and the extremely rare occurrence of granular extrusion "in toto" in some cells, e.g. STH cells, leads to consider a new mechanism of secretion. Agranular cells full of large lysosomes are supposed to be some of the known varieties undergoing elimination of granules and membranes.

HABITUATION OF NATURAL HEAD MOVEMENT IN MAN. A. Gonshor. Aviation Medical Research Unit, Dept. of Physiology, McGill University, Montreal, Canada.

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Habituation is the long term change of response effective from one stimulus period to the next. Previous prolonged oscillatory rotation of humans in the frequency range of natural movement (reliable angular velocity transduction in the semicircular canals) showed no evidence of habituation. The second experimental phase examined whether an intentionally discrepant visual stimulus (mirror-reversed visual world), superimposed upon the non-habituating vestibular one, could generate an habituating response. Results showed that within a day's experimental session the vestibulo-ocular response progressively decreased with incomplete recovery by the next day, indicating a possible long term adaptive phenomenon. To investigate how far this habituating influence can be taken, a system of reversing prisms are being worn by subjects for prolonged periods. The object is to examine quantitatively the development and retention of habituation during and after exposure to the habituating stimulus throughout daily life for up to two weeks. Preliminary results in two day experiments indicate the production of very pronounced and long lasting vestibular habituation.

THE EFFECTS OF AMPHETAMINE AND RESERPINE ON THE REPRODUCTION IN RATS. S. González-Barón. Dept. of Physiology, Univ. of Navarra, Pamplona, SPAIN.

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The influence of amphetamine (1 mg/Kg) and reserpine (0,5 mg/Kg) in both single and repeated doses on the reproduction of rats are studied y determination of both pregnant rats and number of fetus for pregnant it. Amphetamine increases the number of fetus for pregnant rat, when dministered on repeated doses during four cycles. No significative modification on single dose was found. Reserpine decreases the number of fetus on repeated doses. The decrease is most evident for a group of animals to which reserpine had been administered before amphetamine (repeated doses). Administration of reserpine before amphetamine causes a decrease in number of pregnant rats. The results suggest that amphetamine acts partly through an increase in the level of catecholamines, and partly through another mechanism not yet well understood.

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EFFECT OF MUSCLE STRETCHING ON TENSION AND MECHANICAL THRESHOLD DURING CONTRACTURES. H. González-Serratos, R. Valle and A. Cillero. Ctr. of Res. I.P.N., México 14, D. F. MEXICO.

It has been shown that stretching a muscle over its resting length causes changes in its behaviour e.g. an increase of its oxygen consumption, heat production. In the present paper a new type of stretch response is described. The experiments were done with isolated fibres from the semiten-dinosus of the frog (Rana pipiens). An increase in the tension developed during isometric contractures induced with different concentration of potassium was observed by stretching the fibre between 1.17 to 1.64 times its resting length. This was accompanied with a decrease in the mechanical threshold. We attributed this extratension to an increase of the calcium iones released during the activation. This was investigated by exploring the stretch response in fibres being in free calcium Ringer. In this case at 1.17 resting length no tension was developed with 40 mM potassium solution, but at 1.4 resting length a clear contracture was developed. In other experiments the calcium was exhausted with caffeine and the stretch response disappeared completely. If the same fibre was perfused with normal Ringer the stretch response reappeared. Is reasonable to conclude then that this stretch response is due to an increase of calcium during the activation.

NEURONAL ACTIONS OF DRUGS WHICH PRODUCE CATATONIA. J.A. Gonzalez-Vegas & J.H. Wolstencroft. Dept. of Physiology, Medical School, Univ. of Birmingham, Birmingham 15, UK. 622

The drugs bulbocapnine, papaverine and 3,4 dimethoxyphenylethylamine, which have one or more methoxy groups on a benzene ring, produce catatonia when injected i-v. or intraventricularly Interactions of these drugs with putative transmitter substances in the C.N.S. has been tested by the technique of iontophoresis from 5-barrelled micropipettes. The pipettes were inserted into the brainstem of unanaesthetised decerebrate cats in the region of the reticular formation of the pons and medulla. All three drugs were found capable of antagonising the inhibitory action of 1-noradrenaline or dopamine applied from another barrel. Excitatory responses to noradrenaline or acetylcholine and inhibitory responses to acetylcholine or glycine were not affected. It is suggested that antagonism of the inhibitory actions of catecholamines in the C.N.S. might be one of the mechanisms by which drugs produce catatonia.

COMPARISON OF SPONTANEOUS AND EVOKED ACTIVITY IN TWO PREGANGLIONIC SYMPA-THETIC NERVES: CERVICAL SYMPATHETIC AND GREATER SPLANCHNIC. P.M. Gootman and M.I.

Cohen, Albert Einstein Col. Med., New York, N.Y., U.S.A.

The efferent discharges of the left greater splanchnic (Spl) and cervical sympathetic (CS) nerves were simultaneously recorded monophasically (bandpass 0.2-1,250 c/sec) in urethane-anesthetized, gallamine-paralyzed, thoracotomized cats. The discharge in both nerves had common periodicities: a) cardiac cycle modulation; b) central respiratory cycle modulation. In some cats CS discharge had 10/sec periodicity which was the same as, but less prominent than, the 10/sec periodicity in Spl activity (Cohen & Gootman, Am. J. Physiol., 1970, 218: 1092-1101). However, the most prominent periodicity in CS recordings consisted of 30-40/sec waves, which were not present in Spl recordings. The existence of common periodicities at different segmental levels indicates that they originate supraspinally, probably in the medullary sympathetic centers. Moreover, the presence of a specific CS periodicity indicates a degree of dissociation between different types of sympathetic activity. Single stimuli delivered to the medullary pressor center (where high frequency stimulation caused blood pressure rises) produced evoked potentials (waves of increased activity) having different latencies in the two nerves (CS, 20 msec; Spl, 40 msec), as well as different time courses. Thus, both outflow systems can be driven from a medullary integrating center, but there exists a degree of response specificity which might originate at spinal levels. (Supported by USPHS grants NB-03970, NB-5304.)

ROLE OF HYOID-EPIGLOTTIS MECHANORECEPTORS IN GUSTATION. V. Gopal. 624 Dept. of Physiology, St. John's Med. Col., Bangalore, India.

Unit and multifiber activity from glossopharyngeal nerve is modulated by movements of epiglottis-hyoid complex (EHC) in Downward movements of EHC resulting in lowering of the lower jaw by 15-20°, produced 80-150% increase in unit firing and this may be further increased to 150-360% by lowering the jaw to 50°. The increased activity, with some initial dimunition, remains elevated for two to three hours. Further lowering of the jaw beyond 50° decreases unit discharge. Ipsilateratilt of EHC inhibits, while contralateral tilt facilitates the afferent discharge. Activity recorded from laryngeal branch of vagus and hypoglossal nerve (1st spinal) does not show any change on these manipulations of hyoid-epiglottis complex. Closure of the oral cavity inhibits the activity obtained from glossopharyngeal afferents.

EVIDENCE FOR A DIFFERENT KIND OF RENIN REACTION. David B. Gordon. Physiology Research Lab. Veterans Admin. Hosp. San Francisco, California. U.S.A.

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In studying the reaction of rat renin with rat plasma (with no adjustment of pH and no chelating agents added), we have found evidence that an unusual sort of renin reaction occurs. This evidence is of three kinds: 1) the pressor product formed is not freely ultrafilterable, 2) the pressor product formed is highly resistant to plasma angiotensinase, 3) the progress curve of the reaction abruptly shifts from a linear increase of pressor activity with time to a plateau of constant pressor activity. The transition usually occurs after about 10 min incubation at 37°C. In all experiments, pressor activity was measured in the ganglion-blocked anesthetized rat; pressor responses being matched against those of synthetic angiotensin (aspartyl-l angiotensin II). The first two types of evidence suggest that the pressor product formed is different from angiotensin I or II, since these are freely ultrafilterable and are rapidly destroyed by plasma angiotensinase. The third type of evidence suggests that the reaction itself differs from the usual renin reaction, since the latter progresses linearly until a significant proportion of available substrate is used up. The plateau observed is not due to substrate exhaustion since only a small portion of the substrate is converted and, furthermore, addition of more renin causes the reaction to progress further. It is tentatively concluded that, in the absence of acid or chelating agents, renin combines with renin substrate in plasma to form an enzyme-substrate complex which is able to exert a pressor action without complete splitting of the angiotensin molecule away from the parent substrate molecule.

STUDIES ON FATIGUE IN SKELETAL MUSCLE. T. Gordon, O. Hudlicka, G. Vrbova. Department of Physiology, University of Birmingham, Birmingham 15, England.

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The slow soleus muscle in cats fatigues less rapidly than fast muscles. It was recently found that during activity the fast muscles lose considerable amounts of inorganic phosphate (Pi) whereas the slow soleus muscle does not (1). The possibility that the loss of Pi from fast muscle is responsible for fatigue has been investigated. The arterial inflow and venous outflow from a cat gastrocnemius muscle were isolated. The muscle was stimulated via its motor nerve at 2-4pps, and the twitch tension and displacement recorded. In all 21 cats, 8-10 minutes after such stimulation, the work performed by the muscles decreased by 40-50%. However, in 7 of 13 experiments in which Pi was infused during this period by close arterial infusion, the work performed did not decrease. Moreover, rat extensor digitorum longus muscles, stimulated in vitro, ceased to contract in Locke solution (which contains no Pi). Muscles contracting in Krebs-Henseleit solution (which contains Pi), do not fatigue, unless the Pi concentration in the Krebs-Henseleit solution has been lowered. This fatigue effect can then be reversed by adding Pi to the bath. These results suggest that the loss of Pi plays a role in the development of muscle fatigue.

(1) Hilton, S. M., Vrbova, G. J. Physiol. 206: 29P, 1970.

THE TRANSPORT AND NET REMOVAL OF GALACTOSE BY THE INTACT LIVER. C.A. Goresky and B.E. Nadeau. McGill University Medical Clinic, Montreal General Hospital, Montreal, Canada.

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Galactose, a monosaccharide rapidly phosphorylated within liver cells, is irreversibly removed from the portal circulation. We have studied the kinetic relations between hepatic cell entry and the metabolic sequestration process, by means of the multiple indicator dilution technique. Labeled red cells (a vascular indicator), labeled sucrose (an extracellular reference), and labeled galactose were rapidly injected into the portal vein, and from rapidly sampled hepatic venous blood, normalized outflow-time patterns were secured. The labeled red cell curve rises to the highest and earliest peak, and decays rapidly; and that for labeled sucrose rises to a later and lower peak. Its extrapolated recovery is equivalent to that of the labeled red cells. At low blood galactose concentrations, the labeled galactose appears at the outflow with labeled sucrose, but is much reduced in magnitude, and exhibits a low-in-magnitude tailing. Its outflow recovery is much reduced. At high blood galactose concentrations, the initial part of the profile increases towards that for labeled sucrose, and the tailing becomes larger in magnitude. We have modeled the uptake of labeled galactose, and find two predicted parts to the outflow pattern, corresponding to our experimental observations: throughput material, which sweeps past the cell surface in the extracellular space; and returning material, which has entered the cells and escaped the sequestration process. Analysis of the data by use of the model provides estimates of both transmembrane fluxes and rates of sequestration. The $K_{\rm m}$ for the tration is less than 15 mg% whereas that for the entry is approximately 350 mg%. for the seques-

PECULIARITIES OF THE HYPOTHALAMO-HYPOPHYSEAL SYSTEM DURING PUBERTAL PERIOD. T.N.Gorshkova, A.I.Kliorin, A.A.Markossian.Institute of Age Physiology.Acad. of Pedagogical Sciences. Moscow. USSR. 628

The beginning of pubertal period is preceded by intensive changes in the action of Hypothalamo-Hypophyseal System. The increase of excretion of folliculostimulating hormone (FSG) of the hypophysis is expressed more vividly, than of the luteinization hormone. The dynamics in the secretion of hypophysis is to our mind a provement of the leading role of FSG on the initial stage of puberty Perhaps the secretion of FSG is of paramount significance in the stimulation of production of estrogens. With the beginning of formation of the secondary sexual signs, there is found an increase of estrogen production in the overall and in fractions in 8-17 times. There is also an increase of excretion of 17-ketosteroids till 110%. Our researchers showed the presence of parallelism between the pubertal period and the intensity of pigmentation of hair, which is to our mind the result of the increased activity of hypophysis. So we have provements of the fact that the hypothalamo-hypophyseal activity on the initial stage of pubertal period is characterized by the complex of hormonal effects, stipulating the beginning of endocrine situation of this period.

A LIPOLYTIC EFFECT OF CATECHOLAMINES IN RATS ADAPTED TO AN EFFORT IN 629 WATER AT VARIOUS TEMPERATURE. J.Górski, R.Kordecki, K.Kiczka. Department of Physiology, Medical Academy, Białystok, Poland.

Experiments were carried out on 30 male Wistar rats weighting from 200 to 250 g and divided into three groups: lst-control,2nd-adapted for one month to swimming in water at 30°, 3rd-adapted to the same effort for one month in water at 20°. From each of rats three samples of epidydymal one month in water at 200. From each of rats three samples of epidydymal fat tissue were taken and incubated separately according to the method of Schotz and Page. First sample was control one, second was incubated with 3x10-mol of adrenalin /A/ and third with the same concentration of noradrenalin /NA/. The amount of free fatty acids /FFA/ liberated was expressed in project of tissue/3-hour incubation. The following results were obtained: Ist group: control sample-2,65+1,19, /A/-3,46+1,25, /NA/-4,58; 2nd group: control sample-2,96+0,87; /A/-3,12+1,00, /NA/-4,01+1,41; 3rd group: control sample-3,45+1,73, /A/-4,55+1,34, /NA/-7,09+2,19 The results presented indicate that: a/ the adaptation to the physical effort induces changes of the reactivity of the epidydymal fat tissue to the lipolytic effects of catecholamines, b/ the direction of these changes depends on the temperature of water at which the animals were swimming swimming

CHOLINESTERASES IN DIFFERENT PARTS OF THE RAT AND RABBIT PITUITARY. J.L.Gosbee, A.Fisher and K. Lederis, Divisions of Pharmacology and of Morphological Sciences, Faculty of

Medicine, University of Calgary, Alberta, Canada.

The pituitaries of male rats and rabbits were fixed in formalin-sucrose-ammonia, sectioned on a freezing microtome, and subjected to Gomori's thiocholine technique for cholinesterases, using acetyl and butyryl substrates. Eserine and BW284C51 were used as inhibitors. Both acetyl- and butyryl- (pseudo) cholinesterases were found to occur in the pars nervosa and pars intermedia of the rat. In the neural lobe the bulk of the reaction product was deposited along the blood vessels. Occasional nerve fibers could be identified. In addition, comparison with sections stained for neuroglial elements strongly suggested that cholinesterase was also contained in the pituicytes. In the rat pars intermedia the reaction products were restricted to the interlobular areas and to the neuro-intermedia junctional area where strong reactions occured. By contrast the rabbit neural lobe contained little butyryl cholinesterase while acetylcholinesterase was found in fine, apparently single running, nerve fibers. The intermediate lobe showed a strong reaction for both cholinesterases within the constituent cells. These results strongly suggest that cholinesterase-containing structures do not play a comparable role in the pituitaries of the two species examined.

CATECHOLAMINE- AND 5-HYDROXYTRYPTAMINE-CONTAINING CELLS OBSERVED IN THE BRAIN STEM OF CHICKENS. J.Gotoh, H.Ikeda and Y.Kondo. Dept. of Animal Physiology, Fac. of Agriculture, Nagoya Univ., Nagoya, JAPAN.

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In the brain stem of chickens monoamine-containing cells were observed as follows:
(1) 5 clusters of catecholamine-containing cells were observed in the medulla oblongata, 4 clusters in the mesencephalon and 1 cluster in the diencephalon; (2) 5 clusters of 5-hydroxytryptamine(5-HT)-containing cells were observed in the medulla oblongata, 3 clusters in the mesencephalon and 1 cluster in the diencephalon; (3) the monoamine-containing cells distributing in the mesencephalon seemed to supply their axons rostrally to the diencephalon or the telencephalon, while those in the medulla oblongata caudally to the spinal cord; (4) both the catecholamine- and 5-HT-containing cells are suggested to be concerned with autonomic functions, especially with sleep.

STRIATED MUSCLE FORCE-VELOCITY PREDICTION. A. H. Gott, R. F. Janz, M. J. Stimson, The Aerospace Corporation, San Bernardino, California, USA.

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We investigated prediction of cardiac and skeletal force velocity (FV) curves using only active length tension, isometric twitch, passive length tension, and viscosity data. Predicted FV curves match measured non-hyperbolic cat RV papillary and frog sartorius FV curves. Comparison of FV and other dynamic predictions (cumulative change in length, isotonic contraction, quick stretch, etc.) with measured results note systematic variations, observed by Jewell and Wilkie (1958), Wolledge (1966), Yeatman (1969) and others. These patterns suggest pre-load, after-load sensitive active state (AS) dynamic modifications. FV predictions accounting for hypothecated dynamic AS modifications eliminate systematic calculated-measured FV variations. Analyses of sarcomere Ca flow data (Jobsis and O'Connor, 1966; Ebashi, 1968; Ashley and Ridgeway, 1970) demonstrate a plausible relationship between troponin-tropomyosin-actin-bound Ca and tension. Isometric twitch, isotonic contraction, and quick stretch experiments were designed to detect AS modification by aequorin and murexide indication of myoplasm Ca time histories. Closed-loop computer control of muscle, test apparatus, and photomultiplier has been implemented. First results suggest the conclusion that AS dynamic modifications may occur in both cardiac and skeletal muscles.

CHANGES OF THE MALMARY GLAND SECRETORY CELLS MEMBRANE POTENTIAL.

1.1.Grachev. Ukhtomskii Physiological Inst, Leningrad Univ, Leningrad, USSR.

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The mammary gland secretory cells membrane potential, recorded with the help of microelectrode and oscillographic methods is one of the reliable indices of the processes taking place in the cell. Its value is equal to about IO-90 mv. The changes of potential relations of the alveoli lumen and the secretory cells are connected with uneven distribution of ions participating in the processes of active transportation of milk components in the course of the secretory cycle. The experimental findings made it possible to draw a conclusion concerning an important role of acetylcholine and adrenaline in the regulation of the secretory cell function and the participation of oxytocin in the regulation of the ions active transportation process. The pharmacological analysis of the membrane potential with the nerve stimulation revealed the participation of the cholinergetic nerve fibers in the mammary gland innervation. The data obtained suggest the mechanisms of the secretory processes regulation at the cell level.

MODES OF EXCITATORY ACTION OF ASCENDING RETICULAR PATHWAYS UPON HIPPO-634

CAMPAL NEURONS. A. A. Grantyn. Carl-Ludwig-Inst. of Physiology, Karl-Marx-University, Leipzig, German Democratic Republic.

Morphological and physiological findings suggest that ascending reticular netherocal morphological and physiological lindings suggest that ascending reticular pathways responsible for synchronization of hippocampal EEG, after being relayed in septum, exert their action on pyramidal neurons through excitatory synapses located on basal dendrites. Experimental evidence excitatory synapses located on basal dendrites in transmission of for participation of distal axo-dendritic synapses in transmission of reticular basaccampal influences has not as yet been presented. for participation of distal axo-dendritic synapses in transmission of reticulo-hippocampal influences has not as yet been presented. In order to analyse the modes of excitatory effects produced by the stimulation of mesencephalic reticular formation, intracellular recordings were performed from CA2-3 neurons of the cat hippocampus. The excitatory reactions were predominantly of long latency and duration. Increase of discharge rate occurred 1) in association with a sustained or oscillating depolarization amounting to 3-lo mV. 2) without detectable changes of depolarization amounting to 3-10 mV, 2) without detectable changes of the membrane potential. In some cells the generation of full spikes was associated with fast prepotentials, especially during responses of the latter type. According to present knowledge, responses of the 2nd type can be ascribed to activation of "remote" axo-dendritic synapses. It is therefore concluded that both provided and distallar a therefore concluded that both proximal and distal axo-dendritic excitatory synapses are engaged in transmitting reticular influences to CA2-3.

PL CHANGES AT CONSTANT PCO2 AND VENTRICULAR FIBRILLATION. A.O. Grassi, N.F. de Lew and H.F. Cingolani. Inst. of Physiology, Univ.of La Plata, Argentina.

Changes from hypercapnia to hype or normocapnia are known to produce ventricular fibrillation in most species. Similar changes in pl at constant Pco₂ do not seen to cause this arrhythmia because intracellular pl is perhaps not altered in the same extent. Experiments were performed in order to elucidate if changes in pll at constant Pco₂ were able to produce ventricular fibrillation in the perfused heart at 37°C. Heart rate was kept constant by electronic stimulation. Changes in pll at constant Pco₂ were elicited by changing NaICO₃ concentration in the Ringer solution from 5 to 60mM/1, resulting in a change in pll from 6.82 + 0.02 to 7.88 + 0.02, while osmolarity and Na concentration were constant. The mechanical and electrical activity were continuously monitored. The sudden changes in pll produced in 21 runs were continuously monitored. The sudden changes in pH produced in 21 runs of 12 different hearts were accompanied by 15 cases of ventricular fibrillation (70% P(0.01). Our data suggest that changes in pH at constant Pco2 may produce ventricular fibrillation in the rat heart, perhaps through changes in intracellular pll. This findings are consonant with previous data (Cingolani et al. VI World Congr. of Cardiol., London, Sept.1970,p.105) which suggest that changes in pli at constant Pco₂ can influence myocardial contractility in the rat tility in the rat.

REGIONAL VASCULAR RESISTANCE DURING HYPOTENSION AND SHOCK. H. D. Green, R. F. Bond, H. E. 636 Schmid, Jr. and C. E. Rapela. Bowman Gray Sch. Med., Winston-Salem, North Carolina, U.S.A.

Vascular conductances (flow/pressure) were compared during: (a) graded reduction of local perfusion pressure, (b) stepwise hemorrhage and (c) hypo- and normovolemic hemorrhagic shock. In skin, the decreases in conductance during hemorrhage and shock were much greater than that during decreases of local perfusion pressure; the decreases were independent of sympathetic innervation and circulating angiotensin, but depended on a rise in circulating catecholamines. In skeletal muscle and kidney, an autoregulatory increase in conductance accompanied decreases in local perfusion pressure. During hemorrhage this autoregulation was overpowered by sympathetic vasoconstriction and vasoconstrictor hormones. In the cerebral beds only autoregulatory vasodilation (increase of conductance) occurred during all three forms of hypotension. The vasoconstriction in skin and kidney persisted throughout shock; but a "decompensatory" loss of arteriolar constriction, apparently due to local accumulation of metabolites, occurred in skeletal muscle during the late phases of both hypo- and normovolemic shock. Decrease of carotid sinus pressure appears to play a role in the vasoconstriction in kidney, and skeletal muscle, but not in skin. Supported by USPHS grants H-487, H-5392 and H-7842, and grants from the North Carolina Heart Association.

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FACTORS AFFECTING EXERCISE TEMPERATURE REGULATION IN MAN. J. E. Greenleaf and B. L. Castle. Ames. Research Center, National Aeronautics and Space Administration, Moffett Field, California, U. S. A.

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The reproducible increase in deep body temperature during exercise is a physiologically regulated process involving the interplay of the heat dissipation mechanisms and not simply a failure of the latter. Factors other than work rate, ambient temperature and humidity that may contribute to this regulation, namely the absolute versus relative Vo2, body position, mode of exercise and the state of hydration, have been investigated in young men. During exercise at altitude, equilibrim levels of rectal temperature ($T_{\rm re}$) were the same as sea-level values, sweating was increased while mean skin temperature ($T_{\rm re}$) and tissue conductance (K) decreased; thus, sweating was not directly related to either $T_{\rm re}$, $T_{\rm s}$ or K. During intermittent, compared with continuous exercise, sweating and $T_{\rm re}$ were elevated slightly, $T_{\rm s}$ was unchanged while K decreased; thus, sweating did not follow $T_{\rm s}$ or K. With supine exercise, $T_{\rm re}$ was unchanged, but $T_{\rm s}$ and K were increased compared to upright work; therefore, sweating followed $T_{\rm re}$ but not $T_{\rm s}$ or K. With hypohydration, $T_{\rm re}$ and K were increased, sweating was reduced while $T_{\rm s}$ was unchanged; therefore, sweating was not related to $T_{\rm re}$, $T_{\rm s}$ or K. We conclude that during exercise sweating is influenced by a mechanism involving more than a simple $T_{\rm re}$ and $T_{\rm s}$ relationship.

FORELIMB TRANSCAPILLARY WATER MOVEMENT AND SEGMENTAL VASCULAR RESISTANCES IN ENDOTOXIN SHOCK. George J. Grega, W. Jeffrey Weidner, and Francis J. Haddy. Department of Physiol. Michigan State University, East Lansing, Michigan 48823, U.S.A.

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Collateral-free, innervated, naturally perfused forelimbs were used to study transcapillary water fluxes in skin and skeletal muscle in pentobarbitalized dogs (n=10) subjected to endotoxin shock. E. coli endotoxin (5mg/Kg, I.V.) produced sustained decreases in skin and skeletal muscle vascular pressures and flows; segmental vascular resistances (large artery, small vessel, large vein) increased, especially in skin. Forelimb weight decreased 8.5 ± 2.7g by 10 min and 21.7 ± 3.8g by the end of a 4 hour period. The initial rapid weight loss is largely attributable to a decreased vascular volume subsequent to constriction of forelimb capacitance vessels i.e. small vessels and large veins. From minutes 10-240, resistance in the capacitance vessels further increased in skin and decreased toward control in skeletal muscle, the net effect being a fall in total forelimb vascular resistance toward control. This suggests an increasing forelimb vascular volume from minutes 10-240 and hence that the weight loss over this period is attributable to continuous water influx. Small vein pressure was decreased in skin and skeletal muscle (0-240 min) suggesting that the water influx resulted from a fall in Pc. A fall in Pc would result if the decrease in aortic pressure and the increase in precapillary resistance negated the effect of the increase in postcapillary resistance. These data are similar to those following 2 mg/kg, I.V. (Fed. Proc. in press) and fail to support the contention that water efflux into skin and skeletal muscle is a determinant of irreversibility in endotoxin shock.

SINGLE UNIT ACTIVITY IN THE SPINOCERVICAL TRACT UPON STIMULATION OF CUTA-NEOUS UNMYELINATED FIBRES. Gregor, M., II. Physiologisches Inst. Heidel berg, Germany.

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A pure afferent volley in the C-fibres of cutaneous nerves produced by electrical stimulation during a selective block of the A-fibres induce activity in 60 % of the axons within the spinocervical tract. The response consisted of a repetitive discharge at a latency of about 200 ms. This C-discharge exhibited only a weak suppression by a preceding volley in the A-fibres of the same nerve. The probability of C-fibre input was higher in the units monosynaptically activated via A-fibres than in those units with polysynaptic connections. Activity upon a C-fibre stimulus occured at a higher probability (80 %) in units exhibiting a steady state discharge than in units which were silent in the absence of stimulation. In the units activated by stimulation of hairs C-input was present in 55 %, whereas in units activated by sustained skin pressure this prob-

ability was 75 %

(Supported by the Deutsche Forschungsgemeinschaft).

640 INTERACTION OF VIIITH NERVE STIMULI IN THE ASCENDING AND DESCENDING MLF. E. J. Grey and C. D. Barnes. Dept. of Anatomy & Physiology, Indiana University, Bloomington, Indiana, USA.

Bipolar parallel electrodes were placed bilaterally on the VIIIth nerves of cats which, had been decerebrated at the precollicular level and fixed in an Horsley-Clarke head holder. Ascending and descending mono- and poly-synaptic responses were recorded in the medial longitudinal fasciculus (MLF). Test mono-synaptic responses in the descending MLF medial longitudinal fasciculus (MLF). Test mono-synaptic responses in the descending MLF between 5 - 9 msec. and areas of inhibition on either side. Where this facilatory peak between 5 - 9 msec. and areas of inhibition on either side. Where this facilatory peak occurred in time was dependent on the relative strengths of the conditioning and testing occurred in time was dependent on the relative strengths of the conditioning and testing stimuli. Paired stimuli delivered to the same VIIIth nerve revealed completely different stimuli. Paired stimuli delivered to the same VIIIth nerve revealed completely different stimuli. Paired stimuli delivered to the same VIIIth nerve revealed completely different observed with contralateral conditioning could be produced by symmetrical connections observed with contralateral conditioning could be produced by Symmetrical connections involving collaterals of an efferent inhibitory pathway. (Supported by PHS research involving collaterals of an efferent inhibitory pathway. (Supported by PHS research grant NB 07834, Career Development Award NB 34986, and Fellowship Award GM 41650)

VENTRICULAR MORPHOLOGY-SARCOMERE LENGTHS AND GROWTH IN THE RAT HEART.

A. F. Grimm, K. V. Katele and S. M. Klein. Dept. of Histology and of Physiology, Univ. of Illinois, Chicago, Illinois, U.S.A.

Functioning myocardial sarcomere lengths and force generating ability are dependent upon cardiac morphology (due to the non-uniform and thick-walled nature of the ventricles). This relationship was studied in K⁺ arrested-formalin fixed (in situ) hearts from normal rats of different ages and ventricular weights (400-1000 mg). After standard histologic preparation, sarcomere lengths were found to be uniform throughout the ventricles in these relationships in the same also found to be uniform; ventricular growth was proportional. The ratio of left ventricular radius/left ventricular apex-valve distance was the same (at comparable ventrions along the apex-valve axis) for the different hearts. This was true for both internal and external dimensions. The morphology and tension-producing capabilities of the rat heart are apparently maintained during cardiac growth.

CORRELATION BETWEEN SLOW EVOKED POTENTIALS RECORDED FROM THE CAUDATE NUCLEUS (CN) AND A MOTOR CONDITIONED RESPONSE IN CATS. J. Grinberg, R. Prado and H. Brust-Carmona. Psychol. Sch. Univ. Anahuac, México State and Physiol. Dept. Sch. of Med., Natl. Univ. of México, México 20, D. F.

A series of previous experiments indicate that a particular motor conditioned response (CR) depends of the functional integrity of the CN. Thus we decided to record the electrical activity of the CN during the acquisition, maintenance and extinction of the CR. The experiments were performed in adult cats distribuited in three groups. In the first two groups the Ss were conditioned to stay on a platform until the conditioned stimulus (CS) appeared (a light or a sound during 1 sec.) then they walked to the other end of an aisle, got a reward and went back to the platform. When the CR was well established multipolar stainless steel electrodes were stereotaxically implanted in the head of the CN. In the third group the electrodes were implanted prior to the CR acquisition. In the first two groups during the maintenance of the CR a slow potential was recorded. This potential had a duration of 40-60 msec. with an average latency of 80 msec. when the CS was a light or 25 msec. when it was a sound. In the third group as the Cr was being acquired the potential began to appear and grow to become steady when the CR was well established. In all Ss there was a correlation of 0.72 to 0.99 (rs) between the CR and the appearance or the voltage of the potential. The suppression of the US produced the extinction of the CR and a decrement of the amplitude of the evoked potential, but with the restoration of the US both the CR and the potential were reestablished to the previous condition.

PHYSICAL CHARACTERISTICS OF SPLENIC RED CELLS. A.C. Groom and S.H. Song*. Biophysics Dept., Univ. of Western Ontario, London 72, Canada.

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Kinetics of cell washout, when isolated cat spleens are perfused with Ringer solution, show that the red cells stored in the spleen correspond to a system of 3 compartments (fast, intermediate and slow). Morphological studies at different stages of washout identified these compartments as free cells in vascular channels, free cells within sinuses and cells adhering to sinus walls respectively. The question now arises: are the last cells different from the rest in any way? We collected red cells from the slow compartment, after the free cells (fast, intermediate) were washed out, and measured their density (phthalate method), volume and osmotic changes (celloscope). In comparison with arterial cells the splenic cells were 5.6% larger (p = .02), less dense (1.083 vs 1.094; p < .05), and swelled 5% less in 200 mOsm/L (p < .01). The density difference indicates that the splenic cells were 'young' cells. The density was lower than expected if the larger volume were due only to an increase in water content. The decreased swelling at 200 mOsm/L suggests that the splenic cells became spherocytes sooner than arterial cells, i.e. osmotic fragility was probably altered. Therefore it seems likely that the slow compartment represents reticulocytes in the process of maturation. (Supported by MRC grant MA-2586. *Fellow of Canadian Heart Fndn.)

THE FACILITATED DIFFUSION OF CO, IN HEMOGLOBIN SOLUTIONS. G. Gros. Inst. für Physiologie der Med. Hochschule Hannover, Hannover, BRD.

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The CO₂ flux across 150 µ thick layers of hemoglobin solutions was measured in two different CO₂ partial pressure ranges (10/50 and 100/650 Torr respectively). The hemoglobin concentration was varied from 0 to 45 g%. Temperature 22 and 38°C. The CO₂ flux per CO₂ partial pressure difference was up to 80% higher in the low CO₂ partial pressure range than in the high range. The additional flux in the low pressure range suggests a facilitated diffusion of CO₂ confirming observations in hemolysed blood by LONGMUIR, FORSTER and WOO (1966). The rate of facilitated CO₂ diffusion showed a maximum value at a hemoglobin concentration of 20 g%. Comparing the fluxes measured in 4-20 g% hemoglobin solutions we found that the facilitated diffusion of CO₂ per bicarbonate concentration difference was linearly related to the hemoglobin concentration. The temperature coefficient was 6%. Facilitated CO₂ diffusion by bicarbonate diffusion requires an equivalent H transport. It is theoretically shown that the H transport by H diffusion is negligible. The calculated transport of H by hemoglobin diffusion is only 20% of the measured facilitated CO₂ diffusion. The results indicate a special H transport mechanism in hemoglobin solutions.

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BEHAVIOUR OF THE KININFORMING SYSTEM DURING THE BLOOD PRESSURE MODIFICATIONS. L.Grosu, M.Rădulescu, G.Uza. Dept.of Physiology, Inst.of Med. and Pharm., Cluj, România.

Investigations concerning the kininforming system were done in 25 hypertensive patients (H.P.), in comparison with 10 healthy controls. A significant decrease of kininogen (K-gen), an increase of free kinins (K) and an not significant inhibition of plasma kininases were noted in the hypertensive group. Intravenous infusions of angiotensin (A) was found to produce in most of the control subjects a decrease of K-gen and an increase of the fibrinolytic activity. The procedure caused a decrease of the K-gen in only 50% of the H.P. H.P. in which no decrease of K-gen after infusions of A. was noted, were also more sensitive to the hypertensive effects of A. Changes of free K. and kininase activity after infusions of A were not statistically significant. The data suggest that during increase of blood pressure there is a release of K. which might have a compensative role. In order to verify this hypothesis the characters of the hypertensive reactions produced by adrenalin in dogs treated with inhibitors of the kininases was studied. The results obtained so far, do not demonstrate any role of the kininforming system in the moderation of hypertensive reactions, or in the production of post infusional hypotension.

EVIDENCE OF CENTRAL AND PERIPHERAL NEURAL INHIBITION OF THE CONTRACTILE RESPONSE OF THE LACTATING RAT MAMMARY GLAND TO OXYTOCIN IN VIVO. C. E. Grosvenor, D. J. DeNuccio, H. Maiweg, and F. Mena. Dept. of Physiol., Univ. of Tenn. Med. Units, Memphis, Tenn. USA

The intramammary pressure responses (IMPR) to i.v. injections of oxytocin were eval-646 uated before and after nerve section in the urethane-anesthetized primiparous rat. nerves were exposed several minutes before the first IMPR was elicited. Cutting the dorsal roots supplying the 6 abdomino-inguinal glands increased both the slope and amplitude of the IMPR of each ipsi- and contralateral gland caudal to the point of section; the IMPR of glands rostral to the section were unaffected. The IMPR increased similarly after severing the ventral roots but the effect was confined to the ipsilateral glands. The IMPR also increased when the segmental nerves were cut. The slope and amplitude increased immediately after each of the 3 procedures. The increases were small in magnitude (50-60%) but were consistent. The IMPR initially was depressed after transecting the spinal cord at T-10-T-11 then increased dramatically in slope and amplitude over the next 1-2 hours to where each oxytocin dose within the linear portion of the dose response curve produced near maximal IMPR; oscillations in the IMPR also occurred. The IMPR of glands rostral to the transection were unchanged. The IMPR increased in a manner similar to that following spinal cord section when 25% KCl was placed on the cerebral cortices. These results suggest a diffuse motor innervation exists in the rat mammary gland which appears to be inhibitory in function and to be sensitive to peripheral and, more strongly, to central influences. (Supported by USPHS Grant HD 04358 to C.E.G.)

CRITICAL CONDITIONS FOR THE OXYGEN SUPERY OF THE BRAIN DURING RESPIRATORY AND NON-MESSTRATORY ACIDOSIS. J.Grote, M.Kreuscher, P.Vaupel and M.Gunther. Inst. of Physiology and Inst. of Anesthesiology, University of Mainz, Germany.

Dogs were anaesthetized with Non-Dog mixture, relaxed and arteficially ventilated. Respiratory and non-respiratory acidotic states were produced. Mypoxemia was then induced by controlled progressive reduction in the arterial oxygen tension. Simultaneously the total and regional cerebral blood flows were measured. Pog., Pog., pM and the glucose, lactate and pyruvate concentrations were determined in arterial and cerebral venous blood. The Og and glucose uptake and the lactate output of the cerebral tissue were calculated. Under induced arterial hypoxia characteristic hypoxic reactions of the brain occur during respiratory and non-respiratory acidosis at higher arterial and cerebral venous oxygen tensions in comparison to the conditions under normal acid-base state. An increase in cerebral blood flow is noted at cerebral venous oxygen tension between 35 and 40 mm Mg (Reaction Threshold). Critical conditions for the oxygen supply of the brain occur when the oxygen tension of the cerebral venous blood falls to 30 mm Mg (Critical Threshold). An oxygen deficit of the cerebral tissue is demonstrated below the "Reaction Threshold" by an increase in the lactate-pyruvate ratio of the cerebral venous blood.

AGE-RELATED UROPEPSIN REACTION TO STRESS. P.Groza, St. Ionescu, D. Bogatu and N. Cinca. "D. Danielopolu" Inst. of Physiology, Academy of Medical Sciences, Bucharest, Romania.

The present work was intended to study uropepsin elimination under normal conditions and following operative stress in patients aged 9 to 73 years. A certain relation was found between the amount of eliminated uropepsin and age, maximal elimination being noted in the fifth decade. Up to 60 years, surgical stress brought about an elevation in uropeosin removal, followed by a decreased elimination thereafter. The changes observed were more obvious on the first post-operative day. Uropepsin recovered normal levels after approximately 6 days; blood pepsinogen showed similar modifications. These findings reflect a diminished reactivity to stress after 60 years. The relation between stress and uropepsin elimination can be accounted for by the positive effect of glucocorticoids on pepsin secretion. Quantitative assay of uropepsin may serve as a reactivity test to stress.

Ca ANTAGONISM, A NEW PRINCIPLE OF VASODILATION. G.Grün, A.Fleckenstein and Y.K.Byon. Physiological Institute, University of Freiburg, Germany.

The tone of vascular smooth muscle as well as autoregulation (vasoconstrictor responses to graded intravascular pressure increases) is intensified if the extracellular Ca concentration rises, whereas vasodilation occurs in Ca deficiency. The Ca effects are potentiated by an increase in pH and disappear if the pH is lowered. Sympathetic a-receptor blocking agents do not interfere with the Ca actions. A new and specific way of blocking the Ca effects on vascular smooth muscle was opened by the recent discovery of the highly potent Ca-antagonistic properties (1,2) of some drugs such as verapamil, D 600 (a methoxy-derivative of verapamil) and prenylamine. Even small doses of these compounds (1 mg/l or less) cause a large vasodilation and abolish autoregulation in isolated perfused rabbit ears and relax arterial strips; These drug effects can be neutralized or overcompensated by an increase in Ca. Catecholamine-induced vasoconstriction is also inhibited by the Ca-antagonistic compounds but to a lesser extent.

Fleckenstein, A., G.Grün, H.Tritthart and Y.K.Byon: Klin.Wschr. 49, 32-41 (1971)

 Fleckenstein, A., H.Kammermeier, H.J.Döring, H.J.Freund, G.Grün and A. Kienle: Z.f.Kreislaufforsch. <u>56</u>, 716-744, 839-858 (1967)

EQUIVALENT CIRCUIT OF CRAYFISH MEDIAN GIANT AXONS. H. Grundfest, and S. Yamagishi. Lab. of Neurophysiology, Dept. of Neurology, College of Physicians and Surgeons, Columbia University, New York, New York, USA.

The resting potential is determined mainly by K, but when K is absent a ten-fold decrease in Na results in decreased conductance and hyperpolarization of about 30 mV, independently of the permeance of the anion. Hyperpolarization is not blocked by TTX. When both Na and K are absent a ten-fold increase in Ca depolarizes by about 20 mV, provided the anion is impermeant. Despite the depolarization the conductance decreases. Thus, the resting membrane is an electrode for the 3 cations and Cl, with mobilities ranking K > Na > Ca Cl. Except for an after-depolarization (peak ca 5 mV; duration ca 5 msec), spikes are brief (< 1 msec) and nearly symmetrical. They are blocked by TTX or low Na (< 70 mM) and the overshoot changes about 45 mV/decade Na. Thus, both Na and K activation occur during the spike. However, the overshoot changes about 8 mV/decade Ca and the after-depolarization is associated with an increased conductance for Ca. The Cl battery does not participate and spike electrogenesis is due to increased conductance for the 3 cations. The equivalent circuit for the axon thus includes electrically inexcitable passive conductance pathways as well as reactive channels. (Work supported in part by NIH, NSF and MDAA).

REGIONAL BLOODFLOW IN NORMOVOLEMIC EXCHANGE ANEMIA IN DOGS. G.Grupp, Ingrid L. Grupp, J.C.Holmes, and N.O.Fowler. Depts.of Physiol.and Med., Cardiac Lab., Col.Med., Univ. of Cincinnati, Ohio, USA.

To understand more about the mechanism of the card.vasc.consequences and the response of regional bloodflow(BF)to anemia we measured BF in the renal, carotid, and femoral supply areas with sine-squarewave el.mag. BF meters in dogs anesthetized with Morphine-Chloralose. Normovolemic anemia (hematocrit below 20) produced by dextran exchange led to more than doubling in cardiac output (CO), increased heartrate (HR+70 beats/min), and widened pulse pressure. Total periph. Resistance (R) was reduced by 50%. All regional BF we measured increased: carotid and femoral flow more than doubled as did CO:renal BF increased less (+50%); renal R decreased only by 31%. Complete adrenergic blockade with Sotalol or additional muscarinic blockade (Sotalol and Atropine) did not change the BF response to anemia, and CO response decreased only slightly; but Sotalol decreased the HR response significantly and Sotalol+Atropine abolished it. Conclusions: Regional BF, including renal flow, is increased during normovolemic exchange anemia. CO and BF increases occur in the absence of an increase in HR. Since cardiac sympathetic (as is falsely assumed) and parasympathetic activity contribute little to high CO and BF in anemia, attention is focused on physical causes (viscosity, peripheral R, pre-and afterload). (Supported by USPHS HE 06307 and Amer. Heart Ass. SW Ohio Chapter).

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RESPONSES OF NEURONS IN THE CAT'S VISUAL SYSTEM TO MOVING LIGHT-DARK PATTERNS.

O.-J. Grüsser, Ursula Grüsser-Cornehls and D. I. Hamasaki. Dept. of Physiology, Freie Universität Berlin, Germany and Dept. of Ophthalmology, Univ. of Miami, USA.

The responses of concentric receptive field (RF) neurons in the retina and the geniculate body and of complex RF units in the cortical visual area 18 and 19 were recorded. The effect of angular velocity, shape, size and direction on the neuronal response to moving stimuli was investigated. Sinusoidal and triangular spatial oscillation of different amplitude, frequency, and direction was applied to simulate the movement of the retinal image caused by voluntary and involuntary eye movements (tremor, drifts and saccades). At photopic stimulus conditions the maximal response of retinal neurons was reached at an oscillation frequency between 5 and 20 per second, while for geniculate neurons the maximal neuronal response was obtained between 2 and 12 oscillations per second. Movement sensitive neurons in the visual cortex gave a maximal response at an oscillation frequency between 2 and 5 per second. The response of cortical neurons depended further on the amplitude, contrast, and size of the moving target, but only weakly on the average luminance level. For part of the cortical neurons the orientation of the moving border was another important stimulus parameter.

Supported in part by a grant of the Deutsche Forschungsgemcinshaft (Gr.161) and by Public Health Research Grant #07575 from the Natl. Eye Inst., Natl. Insts. of Health, Bethesda, Maryland 20014 USA.

SPONTANEOUS AND EVOKED ACTIVITY OF BULLFROGS VESTIBULAR STATORECEPTORS IN WEIGHTLESSNESS.

FOUR UNITS SAMPLED CONTINUOUSLY DURING A SIX-DAY ORBITAL FLIGHT. Torquato Gualtierotti
and Francesco Bracchi. Ames Research Center, NASA, Moffett Field, Calif., U.S.A.

Permanent Address: II Department of Physiology, University of Milan Medical School.

The pulses from four single vestibular statoreceptors nerve fibers have been recorded

The pulses from four single vestibular statoreceptors nerve fibers have been recorded through chronically implanted microelectrodes (modified from Gualtierotti and Bailey, Electroenceph. clin. Neurophysiol. 25:77-81, 1968) in two semi-paralyzed bullfrogs in the laboratory and during 155 hrs. of orbital flight. A space capsule provided the life support system for the frogs completely submerged in water at constant temperature with the head fixed. The animals were periodically stimulated through a centrifuge (0.6 g). A satellite capable of maintaining less than 10-3 g in all directions has been placed in orbit by a Scout Rocket. The pulses were recorded on the ground through telemetry together with EKGs, water temperature and pressure, accelerations at the frogs head and in the three directions of space. Four different experiment programs were available upon ground command. During flight real time data were analyzed continuously by computer. The true threshold of at least two statoreceptors was determined. The spontaneous firing rate increased significantly in weightlessness from the first to the fourth day in the different units; excitability was also increased. A change from tonic to nearly phasic response was observed at a later stage and eventually such a change disappeared. A trend toward return to normal developed at different times for all units.

654 CEREBELLUM AND ATONIA DURING PARADOXICAL SLEEP. S. Guglielmino and P. Strata. Laboratory of Neurophysiology of the C.N.R. and Institute of Physiology, University of Pisa, Pisa-Italy.

The desynchronized phase of sleep is usually characterized by abolition of the tonic activity of the cervical muscles. It has been shown that sleep atonia is present after cerebellectomy. Our experiments show that following ablation of the entire cerebellum or bilateral lesion of the fastigial nuclei, there is still marked reduction of cervical muscle tonus during the paradoxical phase of sleep, but complete atonia no longer occurs. Brief periods of atonia may be observed only in coincidence with intense bursts of rapid eye movements. The lack of sleep atonia is quite evident during the first week, but usually is still present up to one month after cerebellectomy.

CONTROL EXERTED DURING SLEEP BY PRIMARY SENSORY CORTICAL AREAS UPON THE DIFFERENT SENSORY AFFERENTS. G. Guilbaud, D. Ménetrey, M. Kreutzer and J.L. Olivéras. Physiologie des Centres Nerveux, Faculté des Sciences, Paris 16, FRANCE.

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Associative sensory responses evoked at different CNS levels have been recorded in chronic cats, during wakefulness and the different stages of sleep. The study was made before and after the removal of one or several primary cortical areas. After bilateral removal of one area, the associative responses of this sensory system are no longer affected during wakefulness, fast or slow sleep. For instance, after removal of visual area, the amplitude of associative visual responses are, as in intact animals, large during slow sleep, small during fast sleep and wakefulness. To conclude, during sleep, each primary cortical area seems to control associative afferents only within the same sensory system.

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UPHILL MOVEMENT OF Na AND K IN FROG SKELETAL MUSCLE AT LOW TEMPERATURE (1°C) AND IN THE PRESENCE OF 10⁻⁶ M OUABAIN. <u>J. Gulati, I. Reisin</u>, and <u>G. N. Ling</u>, Dept. of Molecular Biology, Pennsylvania Hospital., Philadelphia, Fa. (19107) U.S.A.

In common with most cells, the frog sartorius muscle has a high K and low Na content. The external medium, in contrast, has high Na and low K. This asymetric distribution of electrolytes in the resting cell has been considered to be a result of the steady state activity of a Na-K pump and an Electrogenic pump. Both pumps are usually considered to be blocked by low temperature and in the presence of ouabain. Our experiments show that the muscle cells are able to accumulate K and exclude Na at 1°C. The cells are first depleted of K by an overnight incubation in a K-free solution. This was followed by 3 days of incubation in the K-free Ringer at 1°C. The final electrolyte composition (µmole/gm wet wt.) of these low-K muscles is K=9 & Na=107. The remaining muscles are now transferred to a 10 mM-K medium at 1°C and the time course of recovery of the tissue K is followed. In this high-K medium, the depleted muscles accumulate K and exclude Na. The tissue electrolyte contents after 48 hrs. are K=59 & Na=68. These levels are maintained up to 94 hrs. of observation. Including 10-6 M ouabain in the 10 mM-K medium has no effect on tissue recovery. The presence of 10-5 M ouabain, however, inhibits the accumulation of K, suggesting a lower sensitivity to the drug at the low temp. These results raise the question whether a pump can still operate at 1°C - the temperature at which it is considered that the metabolic activity of the cells is inhibited. Acknowledgements to John A. Hartford Found. for basic equip. & ONR (#4371(00)1005327) for support. *Fell. C.N.I.C.T. Argentina.

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A COMPARISON OF NORMAL AND INHIBITED CHLORIDE PERMEABILITY IN HUMAN RED BLOOD CELLS. R. Gunn, M. Dalmark, J. O. Wieth and D. C. Tosteson, Dept. of Physiology and Pharmacology, Duke University Medical Center, Durham, N. C., U.S.A. and Dept. of Biophysics, University of Copenhagen, Denmark.

 36 Chloride efflux from human red cells under equilibrium conditions for non-radio-active chloride has been examined in the absence and presence of a series of aromatic anions which reduce Cl^ permeability in the order of potency, trinitrocresolate (TNC) > picrate > salicylate. These inhibitors do not change the activation energy (30 0 kcal/mole-degree, 0°-23° C) or the pH dependence (a two fold increase per unit increase of pH between 6 and 9) of Cl^ efflux. The aromatic anions also inhibit sulfate efflux. However, the pH dependence of Cl^ efflux is different from that of SO4 efflux which decreases with increasing pH (6-9). The rate of Cl^ efflux, 0 0kcl, decreases exponentially with the inhibitor concentration (C) in the medium: ln 0 0kcl, decreases exponentially a constant dependent on pH, temperature, and inhibitor, whereas a = -1.65 for all three anions at all temperatures studied. The efflux of 14 C-salicylate itself decreases steeply when pH is raised from 6 to 7.4, but is unchanged by the presence of the stronger inhibitor TNC. Thus the permeation process of this aromatic anion is different from those of chloride and sulfate. (Supported in part by USPHS research grant HE-12157)

RELATIONSHIPS BETWEEN BLOOD, CEREBROSPINAL FLUID (CSF) AND BRAIN PCO2. G.H. Gurtner, D.G. 658

Davies and B. Burns. The Johns Hopkins Univ., Baltimore, Maryland, USA.

It has previously been shown that steady state differences in PCO₂ (APCO₂) can exist across the alveolar capillary membrane under conditions of no gas exchange, alveolar PCO₂ being higher (Gurtner, Song and Farhi, Resp. Physiology 7:173-87, 1969). The explanation involves movement of [H⁺] from blood buffers towards a negatively charged capillary wall and a slower repulsion of HCO3 away from the wall resulting in a transient production of CO₂ near the wall. In a steady state, the intracapillary ΔPCO_2 between wall and bulk phase is maintained by blood flow past the wall. This mechanism is a general one for weak acids and we found that the weak acids DMO and Barbital were also concentrated in a fluid filled lobe of lung in vivo (Gurtner, Physiologist 12(3):243, 1969). Similar differences in weak acids were found between CSF and blood (Gurtner, Davies and Riley, Fed. Proc. 29 (2):270, 1970). It seems that this mechanism is involved in the regulation of CSF pH (Davies, Fitzgerald and Gurtner, Physiologist 13(3):279, 1970). Measurements of brain tissue PCO_2 using a membrane tipped 500 μ probe connected to a mass spectrometer indicate that ΔPCO_2 between tissue and blood is larger than can be accounted for by metabolic CO_2 production and diffusivity of CO₂ in tissue (Burns and Gurtner, unpublished). It seems possible that the above mechanism might be one which is generally operative between blood and tissue. (Supported in part by USPHS, NIH Grants 5 TO1 MH11110-04 and 5 PO1 HE-10342.)

CATION PERMEABILITY OF HUMAN ERYTHROCYTES IN HYPERTONIC NaCl SOLUTIONS. I. Guth and 659 H. Passow, Max-Planck-Institut fuer Biophysik, Frankfurt (Main), Germany

According to the fixed charge hypothesis, the near impermeability of the RBC to cations is due to coulombic repulsion of diffusible cations by fixed cations in the membrane. The efficiency of the charged membrane to prevent diffusible cations from penetrating can be expected to decrease with increasing cation concentration in the medium. If the fixed charges act by a Donnan exclusion mechanism, the expected increase of cation permeability can be calculated as a function of the ion concentration in the medium. Experimentally, an increase of K^+ -efflux and Na^+ -influx was observed when the NaCl concentration of the medium was raised beyond 4-5 times isotonicity. However, the observed effect was much greater than the predicted effect. A more detailed analysis revealed that the effect cannot only be brought about by electrolytes but also by nonpenetrating non-electrolytes. The effect does not seem to depend primarily on cell volume, since it continues to increase sharply at tonicities at which the cells approach a limiting volume. It is possible to load RBC ghosts with hypertonic KCl solutions. These ghosts loose potassium into hypertonic NaCl solutions of equal tonicity at slow rates which are more compatible with the fixed charge hypothesis than the rates observed in intact cells. Our findings suggest that in intact cells, a minor portion of the cation leakage in hypertonic solution can be related to the fixed charge hypothesis, whereas the major portion is due to some other effect for which no explanation can be offered. (Supported by the Deutsche Forschungsgemeinschaft, SFB 38)

ANDROGEN SENSITIVITY OF THE LEVATOR ANI MUSCLE AND ITS NERVE IN THE RAT. 660 Gutmann and V. Hanzliková. Inst. of Physiology, Czechoslovak Academy Sciences, Prague, Czechoslovakia.

The levator ani (LA) muscle of female rats undergoes postnatally complete involution which can be prevented by perinatal application of testosterone (T.). The muscle is absolutely androgen-dependent and can be tosterone (T.). The muscle is absolutely androgen-dependent and can be maintained in the earliest stages of ontogenesis even after denervation, performed at birth in female rats. During this time the hormone has a relatively nerve-independent action on maintenance of the female LA muscle. The pudendal nerve, losing perinatally its target organ in female rats shows marked retardation of growth and myelination, becomes highly atrophic but is maintained until old age. The nerve is relatively androgen-dependent, T. preventing the early involution and atrophy of the nerve fibres, but only if it is applied perinatally. CORTICAL REPRESENTATION OF THE CONTIONED EYE BLINK IN THE RABBIT STUDIED BY THE FUNCTIONAL ABLATION TECHNIQUE. W. Gutmann, G. Brožek, J. Bureš. Inst. Physiol., Czechoslovak Acad. Sci., Prague, Czechoslovakia.

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Classically conditioned eye blink was established in 8 rabbits by reinforcing visual or auditory CS by corneal air puff (UCS). After the performance reached 90 %, single waves of cortical spreading depression (CSD) were elicited by microinjection of 25 % KCl into the frontal or into the occipital cortex and the slow potential change was recorded with implanted Ag-AgCl electrodes. Frontal KCl injection into hemicortex contralateral to the blinking eye suppressed the conditioned reaction as soon as the negative wave invaded the motor cortex. Recovery started after 6 (8) min. and was completed after 20 (30) min. when using auditory (visual) CS. Occipital injection of KCl into the same hemisphere caused an immediate suppression of the visual CR whereas the acoustic CR was only blocked 2-3 min. later. Recovery proceeded with approximately the same rate as with frontal injection. CSD in the ipsilateral hemisphere had similar but less marked effects. The results indicate that the conditioned eye blink in the rabbit critically depends not only on the intactness of the motor cortex but also on the cortical projection areas of the CS.

BEHAVIORAL AND ELECTROPHYSIOLOGICAL ACTIONS OF CHRONIC ADMINISTRATION OF PROGESTERONE IN THE FEMALE CAT. C. Guzmán-Flores, E. García-Castells, C. Beyer. Depto. de Investigación Científica, IMSS and Inst. de Investigaciones Biomédicas, UNAM, México, D.F., México.

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The effect of progesterone (P) on behavior and brain electrical activity was studied in intact female cats. The EEG and multiunit activity (MUA) of the mesencephalic reticular formation and amygdala during both spontaneous behavior and while interacting with other cats were recorded during a 2 week control period. Daily injections of 5 mg/kg. i.v. of P for 4 days induced intermittent periods of slow wave activity in all structures recorded, while their MUA dropped to a level below that observed during drowsiness. Yet, the cats readily responded to sensory stimulation, although they maintained a relaxed, crouched position. Two days after withdrawal of P the cats became increasingly aggresive attacking other cats when introduced into the observation chamber. During this period the amygdaloid nuclei presented a high tonic level of discharge, which in creased even more with the presence of other animals. The results suggest that P in large dosages induces in the female cat a depressory effect on behavior and brain MUA, and that a period of increased irritability associated with a high level of amygdaloid discharge follows the withdrawal of P.

EXTRA-RENAL FUNCTION OF RENIN: REGULATION OF MATER INTAKE. Y. Gutman, P. Livneh and M. Levy. Dept. of Pharmacology, Medical School, Jerusalem, ISRAEL

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The renin-angiotensin system has been implicated mainly in secretion of mineralocorticoids and autoregulation of flow in the kidney. Both actions of renin cause reduction of Na⁺ excretion and, thus, maintain extracellular volume. Nater intake is another mechanism which can affect fluid balance. The possible relation of the renin-angiotensin system to water intake is suggested by the following experiments.

Hypovolemia did not enhance water intake in nephrectomized rats, while in sham operated rats drinking increased significantly. Isoprenaline and LiCl caused polydipsia in sham operated rats; the response to both compounds was abolished after nephrectomy. Hypovolemia, isoprenaline and LiCl increased plasma renin activity (PRA) in the rat. It is, therefore, suggested that increased PRA was the cause of the polydipsia. The increased PRA caused by isoprenaline was abolished by propranolal and simultaneously the polydipsia discovered.

isoprenaline was abolished by propranolol and simultaneously the polydipsia disappeared.

Renin-like activity has been reported in the submaxillary gland of the mouse. We have found renin-like activity in the submaxillary gland of the rat but no detectable activity in the parotid gland. Water deprivation, hypovolemia, and LiCl caused significant depletion of renin-like activity in the rat submaxillary gland. Extirpation of the submaxillary gland, but not of the parotid, reduced significantly the water intake induced by hypovolemia in the rat.

POTENTIAL FIELDS OF ACTIVE MOTOR UNITS. A.A. Gydikov, D.S. Kosarov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Making use of a new type of surface electrodes combined in plane multielectrodes the volume conduction of the potentials from separate motor
units are studied in human muscles. A method for locating the electrical
centers of the motor units is described. This method is utilized in investigating the extraterritorial potential fields of active motor units.
The time evolution of the potential fields is described concerning symetric and asymetric motor units (according to the place of the motor endplates along the muscle fibres). An unexpected late positivation of the
potential field is observed in the moment of arriving the negative wave
to the end of the motor unit.

MENBRANE CURRENT AND CONTRACTION IN FROG HEART. H.C. Heas and R.Kern. First Department of Physiology, University of Heidelberg, Heidelberg, Germany.

The relation between membrane current, voltage, and contraction was studied in atrial strips using a sucrose-gap voltage clamp arrangement (Haas, Kern & Einwächter, J.Membrane Biol. 2: 180, 1970) and a force-displacement transducer. The experiments were done in normal Ringer's (1.8 mM Ca) at 4° to 7°C. The results are compared to those obtained by Beeler and Reuter (J.Physiol. 207: 211, 1970) on dog ventricular fibres. Frog atria resembles dog ventricle in having a mechanical threshold distinctly higher than the threshold of fast Na inward current and probably identical to that of slow (Na/Ca) inward current (about -30 mV). Peak tension increases with increasing depolarization and reaches a maximum at inside positive potentials. Frog atria differs from dog ventricle in the following points: i) The staircase phenomenon is much less pronounced. There is little change in tension during a series of identical depolarizing clamps. ii) There is no complete relaxation but a sustained contraction during prolonged depolarizations. iii) The magnitude of peak tension does not decrease at strong depolarizations. This holds true for potentials up to +150 mV. The results suggest a more indirect correlation between Ca inward current and tension development in the frog heart than in the mammalian heart.

SEROTONIN IN NORMAL AND TOXAEMIC PREGNANCY. Y.A. Habib, A.A. Gaafer, B.A. Bassouny, M.el Lozy and H.el Banna. Depts.of Physiology and Obstetrics and Gynaeco-

logy, Alexandria Univ., U.A.R.

Serotonin levels in the platelet-free plasma of pregnant women and women in labour were found to be significantly lower than those in non-pregnant controls, while the caeruloplasmin levels in pregnant women were significantly higher than in the controls. This supports the hypothesis that one of its functions in pregnancy is to keep the level of free serotonin in the plasma low, protecting the foetus from the teratogenic and abortificant effects of serotonin. No difference was found between the serotonin levels in pregnancy and during labour, whilst a striking correlation was found between the serotonin levels in the plasma of women in labour and in the umbilical cord plasma of their children, stongly suggesting trans-placental equilibration. In toxaemia, whether eclamptic or pre eclamptic, the serotonin level in maternal plasma, umbilical cord plasma and placenta were very much higher than in the corresponding controls, while there was no correlation between the clinical severity and the serotonin level. In essential hypertension, on the other hand, there was no such rise. Serotonin antagonists (alpha methyl dopa and cyproheptadine) lowered the serotonin level markedly but had no effect on the clinical picture.

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DETERMINATION OF MULTIPLE CARDIOPULMONARY PARAMETERS BY REBREATHING. Jack D. Hackney Clarence R. Collier, and Kishore S. Ambe. Rancho Los Amigos Hospital, Downey, Ca 90242

and University of Southern California, Los Angeles, Ca 90033, USA.

Pulmonary capillary blood flow (QC), diffusing capacity (DL), residual volume (RV) O2 consumption (VO2) and gas mixing were measured by rebreathing a mixture of low concentrations of acetylene, carbon monoxide and neon in air. Neon is simply diluted by alveolar gas. Acetylene and carbon monoxide concentrations change approximately as decaying expo-Others have used breath holding to make similar measurements but we believe nentlals. rebreathing offers ad√antages since multiple trials are not required for each test and it takes less cooperation during exercise. We use a unique multi-chamber sample valve, rapid dual detector gas chromatograph for analysis, and a time share computer program for calculations. Computations assume a single well-mixed compartment. Gas from each of the first 5 breaths is sampled and stored. At a breathing rate of 30/minute, sampling is completed within 10 seconds. Results in normals, at rest, and during several levels of near steady state exercise on a constant-load ergometer, are reproducible and agree with published data. Average relative difference and SD of duplicates: 00.6% ($\pm4\%$); 00.2.8% ($\pm7\%$); DL 5% ($\pm 3\%$); RV 7% ($\pm 5\%$). Average relative error and SD of duplicates: QC 6% ($\pm 4\%$); VO₂ 8% ($\pm 7\%$); DL 5% ($\pm 5\%$); RV 7% ($\pm 5\%$). Average relative error and SD compared to standard methods: DL 0% ($\pm 9\%$); VO₂ -2% ($\pm 10\%$); RV -2% (range -27% to $\pm 24\%$). At different levels of exercise, the relationship between QC and VO₂ is similar to that reported for direct Fick and indicator dilution methods. Our comparisons with standard methods of QC are in progress. We find that in normals this method gives estimates of QC, DL, RV and VO₂ which are reasonable and show appropriate changes due to exercise.

EFFECT OF LOCAL TEMPERATURE CHANGES ON THE VASCULAR RESISTANCE OF THE DOG HINDPAW. J. Hadjiminas. Physiology Dept., Athens University, Greece.

In 15 dogs, blood outflow from the lateral saphenous vein was recorded, 4 cm proximal to the ankle joint, after ligation of all other veins. The paw was immersed in water, whose temperature was varied between 14° and 50° C, at 0.5° - 3°C/min.; water and venous blood temperature and arterial blood pressure were also recorded. Similar arrangements were made and recordings taken from intestinal loops in six other dogs. The vascular resistance of the innervated or acutely denervated hindpaw was lowest at 22° - 31°C and increased considerably (134 - S. E. 7.2 or 257 - 26.0 per cent respectively) at water bath temperatures up to 43°C, but decreased at 44° to 50°C. Subcutaneous infiltration with procaine hydrochloride almost abolished these reactions. The correlation between known thermoreceptor activity graphs and these reactions is close. Such vasoconstriction at 28° to 43°C was not observed in the intestinal loops. So in the hindpaw there exists a regional mechanism protecting the animal from losing or gaining excessive heat, by restricting blood flow, except at temperatures (44°-50°C) damaging to the tissues; then it produces a vasodilation. This local action is probably accomplished through a primitive peripheral nervous network connected to temperature receptor nerve endings.

CHANGES IN THE ADRENAL ACTIVITY UNDER FATIGUE AND THE POSSIBLE ROLE OF SOME MECHANISMS OF REGULATION.I.N.Hadjiolova Inst. of Labour Protection and Occupational Diseases, Department of Work Physiology, Sofia, Bulga-

By means of complex morphological, histochemical and biochemical studies an attempt is made to evaluate the changes in the activity of adrenal cortex in rats under chronic physical fatigue. It has been found an increase in the activity of steroid-3b- ol dehydrogenase and the enzymes of the pentose-phosphate pathway as well as a reduction of the smooth endoplasmatic reticulum in the cytoplasma of the adrenal cells. Changes in the relation between the bound and free plasma corticosterone level were also discovered. The adrenal activity measured by plasma corticosterone level was decreased in the test ani-mals after a new stress condition. It is concluded that some of these changes in the adrenal activity may represent mechanisms of regulation in chronic fatigue.

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MICROPUNCTURE STUDIES OF PAH EXCRETION BY SINGLE TUBULES OF RAT KIDNEY.
D. Haeberle and P. Deetjen. Institutes of Physiology, Univ. of Munich,
West Germany and Univ. of Innsbruck, Austria.

Proximal tubular secretion of p-aminohippurate (PAH) was studied in rats by free flow micropuncture and microperfusion techniques. Results Proximal tubular fluid concentration of PAH depends on 1) PAH-concentration in plasma water, 2) transtubular water flow, 3) length of proximal tubule, 4) contact time. At low plasma concentrations the amount of PAH secreted into that part of the proximal convolution which is accessible to micropuncture is less than 60% of the amount which appears in the distal convoluted tubule. At plasma concentrations above 1 mM/l the rate of secretion of PAH tends to approach saturation (Tm). Constant values for Tm (maximal transport rate), however, cannot be achieved because as concentration of PAH in the plasma increases, the resultant osmotic diuresis decreases contact time between tubular fluid and tubular epithelium

671 COMPLEMENTARY COMPENSATION OF CERVIX UTERI OF MACAQUES AND SPERM TRANSPORT:
E.S.E. Hafez, Dept. Gynecology-Obstetrics, Wayne State University School of Medicine,
Detroit, Michigan, U.S.A.

Comparative anatomy and histology of the cervix uteri were studied in relation to the structure of the penis in crab-eating (M. fascicularis) rhesus (M. mulatta) and stump-tailed (M. arctoides previously known as M. speciosa). In M. mulatta & M. fascicularis the cervical canal is obstructed by one main ventral cervical colliculus and a pair of smaller dorsal colliculi. The dorso-ventral sinuosity of the cervical canal results in marked accumulation of menstrual blood in uterine cavity. In M. arctoides, absence of cervical colliculi and unobstructed cervical canal allows a constant flow of menstrual blood. M. mulatta and M. fascicularis the glans is short, rounded and helmet-shapped. In M. arctoides the glans is long, slender, flattened dorso-ventrally and tapers in breadth. The unusual structure of the vestibule or cervix in certain species may be complementary to the unusual structure of the penis. In species where ejaculation occurs in the cervix or in the uterus the glans penis is slender, tapering as in M. arctoides or the cervix may be short and dialated, as in species where ejaculation occurs in the vagina the glans penis is short and blunt, as in other macaques and man. Complementary compensation of male and female copulatory organs are (a) important for sperm transport in vivo and (b) isolating mechanisms, evolved from natural selection against disadvantageous hybridization with sympatric species or subspecies.

672 ENDOCRINE CONTROL OF FREE AMINO ACID METABOLISM IN UTERINE AND BLASTOCOELIC FLUIDS IN PREGNANT RABBITS. E.S.E. Hafez & St. Jaszczak, Dept. Gynecology-Obstetrics, Wayne State University School of Medicine, Detroit, Michigan

The blastocoelic fluid, uterine fluid and blood serum were collected on chromatography paper strips from different groups of rabbits, 168 hr post coitum: intact untreated or treated with 4 mg/day of progesterone; ovariectomized treated with 4 mg progesterone or 4 mg progesterone +.01 mg estradiol. Eluted amino acides were measured on Spinco Beckman amino acid analyzer. At implantation, concentration of all amino acids in uterine fluids exceeded that of blood serum. Taurine, absent or very low in blood serum and blastocoelic fluid, was found in large amount (170 μ g/g) in uterine fluid. Peaks of molecular N compounds related to choline or histidine were identified in uterine fluid. Concentration of free amino acid in blastocoelic fluid was higher than in blood serum. Blastocoelic fluid contained large amounts of glycine (518 μ g/g), alanine (133 μ g/g) serine (77 μ g/g), glutamic acid (52 μ g/g), glutamine and asparagine (53 μ g/g), threonine (30 μ g/g). Ornithine, aspartic acid, methionine leucine, phenylalanine, tyrosine were found in lowest concentration in blastocoelic fluid. Concentration gradients of different degrees occurred for most amino acids among blood serum, uterine fluid and blastocoelic fluid. Concentration differences between uterine and blastocyst fluids occurred for all amino acids but the degree of gradient varied: maximal gradient was for taurine and minimal for glutamine-asparagine.

THE ACTION OF ETHYL ALCOHOL ON THE RECURRENT INHIBITION IN THE FELINE LUMBOSACRAL CORD. R. Hagenah, J. Meyer-Lohmann, C. Hellweg and R. Benecke. Dept. of Physiology, II, Univ. of Goettingen, Goettingen, German Fed. Rep.

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In experiments on decapitate cats it has been shown (1) that ethyl alcohol exerts a depressant action on the poly- and monosynaptic reflexes. Because the Renshaw cells take part in the control of spinal reflexes, in the present investigations the effect of ethyl alcohol on the activity of single Renshaw cells and on the recurrent inhibition of monosynaptic reflexes was studied in decerebrate and in acute spinalized unanaesthetized cats. Ethyl alcohol (dose: 0,5 - 3,0 g/kg i.v., i.e. 0,5 - 3,0 % blood alcohol concentration) causes a marked increase in Renshaw cell activity tested by antidromic stimulation of muscle nerves, independent of whether the spinal cord is severed or not. In parallel with these findings the recurrent inhibition of the monosynaptic reflexes is enhanced and prolonged. It can be assumed from these results that the well-known disturbances of motor coordination, induced by ethyl alcohol, are partly due to its effects upon spinal levels including the Renshaw mechanism.

(1) Kolmodin, G.M., Acta physiol. scand. 29, 530-537 (1953)

THE ROLE OF ENDOCRINE HORMONES IN OVULATION IN THE RATS. $\frac{N.~Hagino}{USA}$. Section of Neurophysiology, Southwest Foundation, San Antonio, Tex., $\frac{V.~Hagino}{USA}$.

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When PMS was given at 28 days of age ovarian hormones acted on the CNS and subsequently ovulation occurred on day 31. Plasma corticosterone increased on day 29 (47 µg at 8 AM, 78 µg at 3 PM) and sharply declined on day 30 (15 µg at 8 AM, 32 µg at 3 PM). Pituitary FSH content (83 µg/gland at 3 PM) also declined on day 30 (23 µg at 3 PM). Additional ACTH or corticosterone caused an elevation of electrical threshold of the anterior hypothalamus, and subsequently, blocked ovulation. Adrenalectomy allowed a suppression of ovulation; however, substitution of corticosterone in these rats permitted the induction of normal ovulation. In in vitro study, PMS did not increase corticosterone production. However, the rise of plasma corticosterone and pituitary FSH content was suppressed by thyroidectomy. Furthermore, thyroidectomy caused erratic neural activation of gonadotrophin secretion, and subsequently, suppressed ovulation. Substitution of L-thyroxine in these rats permitted the induction of normal ovulation. Therefore, it is concluded that an adequate circulation of thyroid and adrenal hormones in blood has an important role in CNS controlled pituitary system to regulate gonadotrophin secretion.

AN AUTORADIOGRAPHIC STUDY OF THE INTESTINAL ABSORPTION OF FATTY ACIDS. <u>U.Haglund</u>, M. Jodal and O. Lundgren, Dept. of Physiology, Univ. of Göteborg, Sweden.

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The absorption of a watersoluble short chain (³H-propionic acid, PrA) and a lipidsoluble long chain (3H-palmitic acid, PaA) fatty acid from the cat jejunum was compared with the absorption of lipidsoluble ³H-antipyrine (Ap) by autoradiography in in vivo experiments. A segment with a bile-fatty acid solution placed intraluminally was frozen in situ at predetermined times after the tracer administration. The tissue temperature was never allowed to exceed -20° during the autoradiographic procedure. It was demonstrated that I min after the administration of PaA or Ap, autoradiographic grains were found throughout the whole epithelial cell along the full length of the villus although more densely at the tips. Grains were also found in the lamina propria but to a lesser extent than in the cells. Thus a "barrier" for transport of PaA, as of Ap, seemed to exist at the base of the epithelial cells. In experiments with PrA, grains were diffusely distributed throughout cells and lamina propria 1 min after the administration. These observations may be explained by a low cell permeability to PaA and Ap or by a diffusion "hindrance" to lipidsoluble substances caused by the blood flow in the dense subepithelial capillary network. If the latter explanation is true, it strongly suggests that the countercurrent exchange mechanism in the intestinal mucosa is of importance in explaining the different routes of absorption for short and long chain fatty acids.

676 CIRCULATORY REFLEXES FROM LUNG INFLATION. R. Hainsworth*, J. H. Comroe, Jr. and L. Jacobs. Cardiovascular Research Institute, Univ. of Calif., San Francisco, Calif. 94122, U.S.A.

Lung inflation has been shown by some to result in reflex tachycardia, and by others, reflex bradycardia and vasodilatation. In the present experiments, using anaesthetized dogs, and a tracheal divider, we inflated one lung only to different pressures (a) with chest closed, (b) with chest open, (c) (left lung) with lung artificially perfused, and (d) (right lung) with chest closed, left vagus and right aortic nerves cut, carotid arteries perfused at controlled constant pressures, and with vasomotor responses studied in a perfused hind limb.

RESULTS. In most experiments without lung perfusion, inflation of either lung to pressures of 10-40 cm H₂O resulted in tachycardia and hypotension. When a perfused lung was inflated, the typical response was bradycardia and hypotension. In experiments in which secondary responses from arterial baroreceptors were prevented (d), inflation to 10-20 cm H₂O always resulted in tachycardia (average increase at 20 cm H₂O, 17.2 beats/min); inflation to 30-40 cm H₂O always resulted in bradycardia (average decrease at 40 cm H₂O, 68 beats/min). Vasomotor responses were small and variable: usually vasoconstriction at low, and vasodilatation at high inflation pressures.

*Research Fellow of American Heart Association-British Heart Foundation. Supported by NHLI Grant HE-06285.

677 EFFECT OF CELL NA CONCENTRATION ON ALANINE FLUX ACROSS SEROSAL BORDER OF TURTLE INTESTINE. J.J. Hajjar, Department of Physiology, American University of Beirut, Lebanon.

The interaction of Na and amino acids at the intestinal mucosal border has been observed in many animal species. However, little is known about the transport of amino acids across the serosal barrier of the cells. The present investigation deals with alamine efflux from the cell to the serosal solution. The turtle intestine (Testudo graeca) stripped of its muscle layers was utilized and the flux was measured by two methods: (1) An indirect method as described by Curran et al. (J. Gen. Physiol. 46, 1011, 1963) where the time course of approach to a steady state unidirectional flux was measured after the addition of H-labeled alamine to the mucosal solution. (2) A direct method where the tissues were loaded with labeled alamine and the appearance of isotope in nonlabeled serosal solution was determined. The fluxes of alamine were measured under three conditions; normal tissue (pre-incubation in Ringer's solution, Na-loaded tissue (pre-incubation in 10-5m ouabain) and low Na tissue (pre-incubation in choline chloride Ringer's solution. The results show that alamine efflux from the cell to the serosal solution is independent of cell Na concentration. (Supported by the American University of Beirut.)

678 EFFECTS OF LUMINAL PRESSURE ON INTESTINAL FLUID TRANSPORT IN VIVO. A.A.

Hakim, C.B. Papeleux, J.B. Lane, and N. Lifson. Department of Physiology,
University of Minnesota, Minneapolis, Minnesota, U.S.A.

The Wells clamp was used to study relationships between luminal hydrostatic pressure and fluid transport by dog jejunum $\frac{in}{in}$ $\frac{vivo}{vio}$. The rate of absorption from Ringer fluid was unaffected by raising the luminal pressure from 0 to +30 cm H₂0. In contrast, this net fluid absorption was changed to net secretion by negative luminal pressures of 20 to 30 cm of H₂0. Greater negative pressures can elicit copious secretion and obviously cause structural damage. The results with isosmotic Na₂SO₄ solutions were similar except that in the positive pressure range fluid transport was negligible and smaller negative pressures caused net secretion. These findings are essentially similar to those for dog intestinal mucosa $\frac{in}{vitro}$. The mechanism of the $\frac{in}{vitro}$ relationships is almost certainly as follows: Negative luminal pressure increases the normally low hydraulic permeability of the intestinal epithelium (structural change?) so that a pressure difference across the epithelium which would otherwise produce only trivial secretory filtration can now bring about high rates of such filtration. The correspondence with the $\frac{in}{in}$ $\frac{vitvo}{vitro}$ relationships strongly suggests a similar mechanism $\frac{in}{in}$ $\frac{vivo}{vivo}$. The results may be pertinent to the mechanism of some types of intestinal dysfunction.

REGIONAL TISSUE BLOOD FLOW DURING COLD EXPOSURE OF THE NEWBORN LAMB. J.R.S. Hales, G. Alexander & A. Bell. C.S.I.R.O., Ian Clunies Ross Lab., Prospect, N.S.W. Aust.

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In conscious lambs less than 2 days old, blood flow (\dot{Q}) to various tissues was measured by determining the fractional distribution of cardiac output using microspheres 50 ± 10 μ in diameter labeled with Sr-85, Ce-141 and Cr-51. During the maximum metabolic response to cold, cardiac output increased by 50-100% and metabolic acidosis developed. \dot{Q} to the perirenal, inguinal, pericardial, prescapular and cervical fat showed a 5 fold increase, while that to the longissimus dorsi, trapezius, and biceps femoris muscles showed 8, 6 and 3 fold increases respectively. There was a decrease in \dot{Q} to the skin of the leg, ear and midside, nasal turbinates and mucosa, thyroid, kidney, spleen, stomach, small and large intestine, liver and lungs. There was an increase in \dot{Q} to the tongue, diaphragm, intercostal muscles, adrenal, and heart. Both the mean total brain \dot{Q} and \dot{Q} to the hypothalamic area showed small and inconsistent changes. Mean total spinal cord \dot{Q} decreased slightly. The results support the contention that thermogenesis in both fat and skeletal muscle is very important in the newborn lamb exposed to cold. Changes in \dot{Q} to the other tissues correlates with known functions in the cold animal.

RELATIONSHIP OF MOLECULAR WEIGHT TO THE HEMATOLOGIC, ARTHRITOGENIC AND VISCERAL EFFECTS OF DEXTRAN IN THE RAT.* C. E. Hall, S. Ayachi and O. Hall. Department of Physiology, University of Texas Medical Branch, Galveston, Texas, U.S.A.

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Our previous studies have shown that the intraperitoneal injection of certain dextrans produces in the rat a syndrome of anemia, hypocoagulability of blood, infiltration of the reticulcendothelial system (RES) and arthritis. In the present experiment five dextrans ranging in molecular weight from 50,500 to 238,000 were compared. Hemograms and histologic studies revealed that three, having molecular weights of 113,000 and above, caused severe anemia, frequent spontaneous hemorrhages and extensive infiltration of the RES: two of them with molecular weights of 113,000 and 141,000 also caused arthritis of hind paws. A sample of 72,000 MW caused only slight anemia and RES infiltration. The smallest caused very mild anemia, the most pronounced RES infiltration of any dextran and severe arthritis. In general, the degree of anemia was directly proportional to the molecular weight of the polymer used, although pseudoagglutination of erythrocytes occurred only in rats given dextrans of 113,000 and above. RES infiltration, particularly hepatosplenomegaly, was greatest with the smallest polymer and of about equal severity with the others. The results indicated that the arthritogenic effect was not necessarily associated with the hematologic response and that RES infiltration was independent of both.

*This study was supported by a grant HE 08054 from the USPHS.

C-FIBRE ACTIVITY IN THE ELECTRICALLY EVOKED COMPOUND POTENTIAL RECORDED FROM HUMAN SENSORY NERVE FASCILES IN SITU. Rolf G. Hallin and H. E. Torebjörk. Dept. of Clin. Neurophysiol., Academic Hosp. Uppsala, Sweden.

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The compound response to electrical stimuli applied to a fingerpulp was recorded from sensory nerve fascicles supplying the human hand using the microneurographic technique introduced by Vallbo and Hagbarth (1968). The compound potential contained groups of components which were recruited successively at increasing stimulus strength so that components with short latency corresponding to conduction velocities of about 70-30 m/sec were excited when the electric shock was just perceived by the subject, whereas late deflections corresponding to propagation velocities as low as 1.5-0.5 m/sec generally were not recruited until a sensation of pricking pain was experienced at each stimulus. Prolonged compression of the nerve abolished the first part of the response, whereas the late waves remained. Injection of 1% Lidocaine proximal to the recording site producing analgesia did not affect the intrafascicular nerve response, whereas a deposition of 0,25% Lidocaine between the stimulating and recording sites abolished the late waves. It is concluded that activity in both myelinated and unmyelinated fibres is represented in the compound nerve response. Selective blocking manoeuvies, checked with microneurographic recordings in alert subjects, offer a direct way of studying the sensations aroused by activity in various populations of sensory fibres, including those in the C-fibre range. Ref.: Vallbo, A.B. and K.-E. Hagbarth, Experimental Neurology 1968. 21.270-289.

INFLUENCE OF VENTROMEDIAL HYPOTHALAMIC LESIONS ON COMPENSATORY HYPER-TROPHY OF ENDOCRINE GLANDS. L. Halmy and Cs. Nyakas IV. Med. Clinic and Research Division, Postgraduate Medical School, Budapest, Hungary.

Compensatory adrenal, thyroid and ovarian hypertrophy was studied in rats with ventromedial hypothalamic lesion. All surgical interventions were performed in one stage of operation and the rats were sacrificed on the 14th postoperative day. A marked increase of both food intake and body weight had been observed after ventromedial hypothalamic lesion. There was no significant difference in the degree of compensatory hypertrophy of endocrine glands between ventromedially lesioned and sham-operated groups. It was concluded that development of hypothalamic obesity does not interfere with the control of pituitary trop-hormone release at the level of the closed loop feed-back regulation.

HEMODYNAMIC CHANGES, IN DOGS WITH PORTA-CAVA SHUNT DURING HEMORRHAGE.

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Univ. Budapest, Hungary.

Hemorrhagic shock was produced by standard methods in dogs under Chloralose anesthesia. One group without preoperation served as control, in another group porto-caval shunt was estabilished 14-25 days before the actual experiment. Cardiac output and its fractions were followed by thermodilution method, systemic arterial and the central venous pressure by electromanometer, heart rate by ECG, oxygen consumption and carbon dioxide production by Diapherometer. It was found that survival of the preoperated group was significantly higher /90%/ than that of the control group /50%/. During the bleeding periode there were no major differences in the parameters recorded between the two groups but after retransfusion the cardiac output was higher in the preoperated one.

+/Surgical Clinic, Med. Univ. Szeged, Hungary.

THE EFFECT OF ADMINISTRATION OF EXOGENOUS ATP ON THE INDUCTION OF EXPERIMENTAL HYPERTENSION IN DOGS. H.Hamdi. Physiol.Dept.Faculty of Med.Cairo Univ., U.A.R.

Removal of one kidney, followed by partial occlusion of the renal artery of the other, 20 days later, was performed on 26 dogs. 100 mg ATP sodium were i.m. injected daily in 12 animals, while the rest of the animals were used as controls. The arterial B.P. of the non-medicated dogs increased from a mean of 108 ± 11.4 to 160 ± 14.1 on the 7th day. The maximum B.P. reached was 175 ± 7.1 on the 20th day after renal ischaemia. The hypertension was associated with a significant increase in blood urea, serum Na and inorganic phosphate and a decrease in serum K. All the control animals died within 30 days of the induction of renal ischaemia. On the other hand the ATP-medicated animals showed a maximum rise of B.P. of 132.5 ± 11.8 on the 7th day. Thereafter the B.P. declined to the original level. The above cited changes in blood were significantly reduced under the influence of ATP. None of the medicated animals died for as long as 62-80 days when they were sacrificed for histological examination.

INSECT VISUAL PIGMENT SENSITIVE TO ULTRAVIOLET LIGHT. K.Hamdorf, J.Schwemer, M.Gogala. Inst.f.Tierphysiologie der Ruhr-Universität, Bochum-Querenburg, Germany.

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From insect eyes, an u.v.-visual pigment "A"(\$\lambda\$max 345 nm) was extracted by 2% aqueous digitonin (pH 5.2). By u.v.-irradiation, A is converted to a stable product "B"(\$\lambda\$max 480 nm), which reconverts completely to A when by steps to 9.3, the absorbance at 480 nm decreases continously, while the absorbance at 375 nm rises proportionately, owing to the formation of a third pigment "C".Experiments with NH_0H lead us to the assumption that retinal is the prosthetic group of this pigment.-Microphotometric with the results found on solution. - The sensitivity of the receptor sun's spectrum is much higher than that of u.v.-radiation,all molecules visible light quanta. - This work was supported by the Deutsche Forlavia (M.G.).

EXPERIMENTAL PRODUCTION OF THE SYNDROME OF HYPERLIPIDEMIA, HYPERINSULINISM AND OBESITY IN MONKEYS. C.L. HAMILTON, L. Feng and P.T. Kuo. Veterans Administration Hospital and University of Pennsylvania, Philadelphia, Pa. USA.

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In our laboratory, 10 to 15 year old monkeys (Macaca mulatta) manifest abnormal carbohydrate-lipid metabolism after they become obese. While susceptible animals may develop obesity and its attendent metabolic consequences with advancing age, overeating and obesity with similar metabolic abnormalities can be promptly induced in animals of all ages by well-placed hypothalamic lesions. During the earlier periods of overnutrition, the metabolic changes include: obesity, elevated plasma beta and pre beta lipoproteins, (accounting for hypercholesterolemia and hypertriglyceridemia), high fasting serum insulin level and diminished insulin response to glucose loading. Blood sugar levels and glucose tolerance generally remain within the normal range at this stage. Later, with the onset of overt diabetes, there is: hyperglycemia, a lowering of the fasting serum insulin level, flat insulin response to glucose loading, and exaggeration of hyperbeta lipoproteinemia to produce serum cholesterol and triglyceride elevations. Since an essentially similar lipid-carbohydrate metabolism abnormality is frequently demonstrable in atherosclerotic patients, this preparation may serve as a model for the investigation of metabolic mechanisms in atherosclerosis.

ELECTROCARDIOGRAPHIC TIME INTERVALS AS A FUNCTION OF WORK CAPACITY.
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Dept., Salford Univ. England.

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Analyses of the time components: P-R, R-T and T-P of the electrocardiogram have been related to heart-rate (R-R) and work-rate during continuously increasing work-rate tests of work capacity of cyclist athletes on Müller type cycle ergometers. During the linear (work tolerance) phase, the first part of the test, decrease in R-R (increase in heart-rate) is achieved by a related decrease in T-P (cardiac diastole) interval. Both these work-rate relationships fit a linear equation: y=a+bx. This linearity changed to curvilinearity (work stress - Brooke, Hamley & Thomason, 1968. J.Physiol.197,61P) after 55% of the total work to work capacity. Testing both R-R and T-P relationships to work-rate by the method of polynomial curve fitting showed that both conform to curvilinear equations of y=axⁿ but that the P-T (cardiac systole) relationship remained linear. As functions of work capacity the curvilinearity of R-R and work-rate gave correlation r=0.950, but T-P and work-rate gave correlation r=0.996. Beat by beat analysis of all the time components demonstrates that during the curvilinear (stress) phase of the test, the T-P interval oscillates and this is offset by an opposite oscillation in P-T interval. This oscillatory effect was most marked in those cyclists with greatest capacity for work.

THE EFFECT OF HEAT STRESS ON JAPANESE, CHINESE, AND CAUCASIAN HIGH SCHOOL STUDENTS LIVING IN A TROPICAL CLIMATE. I.F.G. Hampton. Dept. of Physiology, Univ. of Hawaii, Honolulu,

Comparisons between racial groups of their thermoregulatory function during heat stress are often clouded by co-existing differences in, for example, age, body size, health, nutritional patterns, or habitual activity. In the present experiments the response to heat was studied in 42 male Chinese, Japanese and Caucasian high school students (mean age 15.6 yr; height 170.8 cm; weight 58.1 kg) of life long U.S. nationality, and closely similar life styles. The findings were compared with measurements from 33 male adults (mean age 25.6 yr; height 176.6 cm; weight 72.55 kg). All subjects were examined using the age 25.6 yr; height 176.6 cm; weight 72.55 kg). All subjects were examined using the Physiol. 1967, 23, 267-275. This involves dressing the subject in a plastic suit sealed at the neck, warming him until a deep body temperature of 38°C is attained, and then maintaining body temperature at this level while measuring the sweat produced and recording other physiological variables. The mean sweating rates during 40 minutes of controlled hyperthermia were students 356 g/hr; adults 486 g/hr. For the different racial groups the rates were Chinese 268 g/hr, Japanese 326 g/hr, Caucasian 466 g/hr. All groups showed similar rates of sweat suppression, and the comparisons were unaffected by differences in body size. Since the Caucasian students showed the greatest, and the Chinese the least, inclination for athletic activities it is concluded that the difference between the groups were due to acclimation status, rather than to a specific effect of age or race on the thermoregulatory response to heat stress.

THE EXTRACELLULAR RECORDED RECEPTOR POTENTIAL OF THE ISOLATED MAMMALIAN RETINA AND THE INFLUENCE OF OTHER POTENTIAL SOURCES ON IT.

R. Hanitzsch. Carl-Ludwig-Inst. für Physiologie, Karl-Marx-Universität, Leipzig, DDR.

At the isolated rabbit retina it is possible to separate the components PIII and PII of the ERG intraretinally with the aid of microelectrodes. The component PIII is mainly receptor potential. But under certain stimulus conditions as repeating stimuli every 2,5 sec.a fast peak is superposed on the receptor potential. This fast peak has its origin more proximal and increases with frequent repetition of stimulus. From similarities between this fast peak and the a-wave of ERG it is suggested that under special stimulus conditions the a-wave represents not only receptor activity. This seems to be valid in rabbit - less in cat.

690 CORRELATION BETWEEN CATECHOIAMINES AND SEROTOMIN CONTENT OF BRAIN STRUCTURES AND BIOELECTRICAL ACTIVITY OF THE BRAIN IN RABBITS.

J. Hano. J. Stach. J. Vetulani. J. Trabka & Słominska-Zurek. Inst. of Pharmacology of the Polish Academy of Sciences, Kraków, Poland.

In immobilized by gallamine rabbits the influence of a dopamine-B-hydro-xylase inhibitor on the above mentioned phenomena was measured. The early effecti.e.30 min.after i.p.administration of 100 mg/kg b.w. of dimethylditiocarbamate was the positive linear correlation of dopamine increase in Hypothalamus and the enhancement of the allert index in the EEG without any other significant changes of dopamine in another brain structures and without any changes in noradrenaline and serotonine content in Hypothalamus Hippocampus and Caudate.ss compared with controls. The late effects i.e. 120 min.after i.p.injection were: dopamine - no more difference in Hypothalamus as compared with controls increase in Hippocampus, insignificant in Caudate; nor-adrenaline - diminished in Hypothalamus and Hippocampus; serotonine - no change in comparison with controls. The alert index quite like in controls. It may be supposed that the main or even the only out of 3 amines stimulateing the EEG patterns is dopamine.

Na +K -ATPase AND GASTRIC ACID SECRETION. T. Hansen, S.L. Bonting, J.F.G. Slegers. Dept. of Biochemistry, University of Nijmegen, Nijmegen, The Netherlands.

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Ouabain inhibits function of lizzard gastric mucosa in the Ussing chamber. When applied to the mucosal side, the potential across the mucosa is decreased within minutes, while the acid secretion begins to decrease only 2-3 hrs later. Application on the serosal side reduces both potential and acid secretion simultaneously. Ion substitution experiments and amiloride effects suggest a net Cl flux from blood to lumen and a net Na flux from lumen to blood. Ouabain appears to abolish the latter flux. Presence of the ouabain-sensitive Na-K activated ATPase (0.2 mole/kg dry wt/hr) was demonstrated and its properties determined (optimal Mg/ATP ratio I; half-action by 5.5 mM Na and I.I mM K; optimal pH 7.2; pl_50 ouabain 7.0). Short-circuit current data indicate a ratio of nearly 4 cations transported per mole ATP. Intracellular changes in cation levels due to ouabain were observed: an increase in Na from 89 to 131 mM and a decrease in K from 80 to 37 mM. Conclusions are that the Na-K ATPase system is responsible for maintenance of cation gradients and active Na flux, while the active H secretion is coupled to the system.

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THE SHAPE, STRUCTURE AND FUNCTION OF THE CRISTA AMPULLARIS. Y. Harada. Dept. of Oto-Rhino-Laryngology, Hiroshima Univ. Sch. of Medicine, Hiroshima, Japan.

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The anterior and horizontal semicircular canals of frog were isolated together with the corresponding ampullar branches of vestibular nerve in Ringer solution. The tip of micropipette was introduced into the cut end of crus commune. The two ampullar receptors were stimulated with a device which could make both ampullofugal and ampullopetal flows. On aspiration of the content of ampullas (ampullopetal stimulation), increase of nerve impulse frequency from horizontal ampullar nerve was recorded, but anterior ampullar receptor did not respond. Whereas on oppressing the content of ampullas (ampullofugal stimulation), response of the anterior ampullar receptor was recorded..... The Ewald's law was proved by this experiment. Next, the shape and fine structure of crista ampullaris were observed in vivo under microscope; the sensory hairs were projected from the crista, but cupula could not be apparently recognized in frogs. Under the observation with electron microscope, only Type II cells and supporting cells were found on the sensory epithelium of the crista of frog. By the scanning electron microscope studies, the surface of the ampullar sensory cells was seen in detail to be provided with large numbers of sensory hair.

THE EFFECT OF SYMPATHECTOMY ON TISSUE LOSS FOLLOWING EXPERIMENTAL FROSTBITE OF THE RABBIT EAR. Esther Hardenbergh. Naval Medical Research Institute, Bethesda, Md. 20014 USA

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The effect of sympathectomy as treatment for experimental cold injury was evaluated by using a standard procedure of such character that the exposed tissue survived if treatment was instituted, but was lost if no treatment was given. New Zealand rabbits were anesthetized ip with either pentothal (40 mg/k) or chloralose-urethane (1 to 10, 75 mg chloralose /k); the shaved depilated ears were immersed to a depth of 3 cm in a cold bath of ethanolethylene glycol-H2O-solid CO2 at -25 C where they were kept for 2 min after freezing had occurred; then thawed. The left ear was rapidly rewarmed immediately in a water bath, 42 C; the right ear allowed to thaw spontaneously in air at room temp. Sympathectomy of the right ear, by excising the superior cervical ganglion and cutting the anterior and posterior auricular nerves, was performed 1 to 20 hrs after cold injury. Recovery was followed until all necrotic tissue had been lost and the wound healed, about 30 days. There was no loss of tissue in ears which were rapidly rewarmed. In slow-thawed, untreated ears all the exposed tissue was lost in almost all cases. Sympathectomy was effective in slow-thawed ears if performed immediately after cold injury, 85% survival; 50% survival, 8 hrs after; 35%, 20 hrs after. Other points noted: some "hot" untreated slow-thawed ears did not lose in the survival of the surviva not lose injured tissue; sympathectomy was not effective if the auricular nerves were not cut. In summary, in these experiments, sympathectomy performed immediately following cold injury was effective in preventing tissue loss. (Supported by Bureau of Medicine and Surgery, Navy Department, Research task MR 005 04 0102A).

ANALYSIS OF SOME HISTOCHEMICAL AND ULTRASTRUCTURAL ASPECTS OF NEURONS AND GLIA USING X-RAYS AND RESERPINE AS EXPERIMENTAL TOOLS. N.I.Harir 1.0.i.Tuncer.S.Falakali.Y.Aksu. Inst. of Physiology, Pathology, and Morphology, Ege University, Medical Faculty. Bornova, Izmir, TURKEY.

Present investigations are designed to study the biology of the nervous system in health and disease. X-rays are one of the experimental procedures that induce alterations on the nervous tissues. In this study the heads of anaesthetized and unanaesthetized adult rabbits were exposed to damaging or small amounts of x-rays. The alteratized adult rabbits were exposed to damaging or small amounts of x-rays. The alterations were detected by acridine orange and electron microscopic techniques. Damaging the effect of x-rays on DNA and RNA of neurons and glia; ultrastructural alterations such as intracytoplasmic vacuolation, disternae in endoplasmic reticulum, dense bodies, deas intracytoplasmic vacuolation, disternae in endoplasmic reticulum, dense bodies, dense intracytoplasmic vacuolation, disternae in endoplasmic reticulum, dense bodies, dense enlarged nucleus, thickened basement membrane, enlargement of spaces between endothenlarged nucleus, thickened basement membrane, enlargement of spaces between endothenlar cells were observed. Pre-treatment with reserpine before irradiation seemsto act protective against radiation injury. It is concluded that reserpine affects the metabolic activities of some nervous tissue cells, e.g. amine metabolism etc. The research is still in progress.

till in progress.
This research is partly supported by The International Atomic Energy Agency.

SOME CHARACTERISTICS OF THE VISUAL AVERAGE RESPONSE IN NORMAL SUBJECTS.

T. Harmony, J. Ricardo, G. Fernández, G. Otero and F. Valdés.

Neurophysiology Lab. Natl. Res. Ctr., Havana, Cuba.

Visual average responses are being widely used as a diagnostic procedure in neurological pathology. Interindividual variations of such responses make comparative studies very difficult. The analysis of fundamental frquencies of these responses and of the symmetry between potentials of homologous areas in normal subjects would be useful as normative data for their study in neurological patients. Bilateral frontal, parietal, temporal and occipital monopolar and bipolar visual average responses were studied in normal adults. Peak latencies of the different waves showed a concentration at 50, 75, 100, 112.5, 125, 175 and 200 msec independently of their polarity in all the sites studied. From the analysis of the autocorrelogram and autospectrogram of each visual average response, the presence of an harmonic of the alpha fundamental frequency is assumed as an important factor in the configuration of the visual average response. Correlation coeficients showed a high degree of symmetry between left and right occipital and parietal areas and a lowest symmetry between temporal areas.

Effect of elevated renal venous pressure on the intrarenal distribution of blood flow.

L. Harsing, G. Köver and L. G. Harsing, Jr. Dept. of Physiology, University Medical School, Budapest, Hungary.

Experiments were carried out in non-diuretic, chloralose anesthetized dogs to investigate the effects of increased renal venous pressure on the intrarenal circulation. Venous pressure was elevated to 30 mm Hg by partial venous occlusion on the left side, the right kidney served as control. Total renal blood flow (TRBF) was measured directly by collecting the venous outflow, cortical and medullary blood flows were also estimated by tissue extraction of Rb (Rb - RBF). TRBF remained unchanged while Rb - RBF fell in proportion to the decreased net hydrostatic pressure difference across the kidney; medullary flow decreased in excess of the cortical. Such discrepancy between TRBF and Rb - RBF was not found in the controls. A reduction of blood flow as determined by the extraction of Rb may be explicable by a shift in both cortical and medullary perfusions towards juxtamedullary channels. Changes in GFR and in PAH extraction provide supporting evidence for this explanation.

EFFECT OF HUMAN CHORIONIC GONADOTROPIN ON THE EVOKED POTENTIALS AND THE SELF-STIMULATION BEHAVIOUR IN RATS. G. Hartmann, Gy. Telegdy, K. Lissák. Inst. of Physiology, Univ. Medical School, Pécs, Hungary.

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The acute effect of human chorionic gonadotropin /HCG/ was studied on the evoked potentials and the electrical activity of the cortex, the hippocampus, the medial and lateral hypothalamus and the mesencephalic reticular formation in ovariectomized rats. The evoked potentials was elicited by electrical stimulation of the cervix and the skin. The results showed that HCG increased the amplitude of the evoked potentials and enhanced the spindle formation on the REG recordings by 0,5-3 hours following hormone administration. In the self-stimulation experiment the stimulatory electrodes were implanted in the medial forebrain bundle and the rate of lever pressing was registered before and after intravenous HCG administration. Immediately after the hormone injection the rate of lever pressing decreased and 0,5-1 hour latter increased. The results indicate that HCG induces a change in the brain excitability.

EFFECTS OF DIETARY Na ON KIDNEY DYE TRANSIT. Rodney B. Harvey, Dept. of Physiology, Univ. of Minn., Minneapolis, Minnesota, U.S.A.

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B6D2F1 adult male mice were fed chows of identical composition except for Na content for 5 days or more with H₂O ad lib. The passage of FD & C Green #3 through structures in renal hilus, surface of cortex and exposed papilla was recorded using previously described photographic methods. Dye was injected into the inferior vena

imeaporis, Minnesota, U.S.A.		
	Peak transit	times sec
Structure 29g	Na/Kg Chow 1	.6g Na/Kg Chow
Cortical CAP	2.9	3.0
Vein-Artery	2.1	2.2
VR -CAP	6.6	5.4*
PcT-CAP	7.0	7.0
DcT-CAP	31.	29.
LLH-CAP	43.	39.*
UNa	.33M	.081M*
UOA	1.3 osm	1.8 osm*
Body Weight	24.7g	25.48
*denotes significa	ant difference	of mean p<.02
denotes significa	THE GILLETERCE	or mean produ

cava at time zero. High Na chow feeding resulted in prolonged transit through vasa recta and long loops of Henle, increased urinary [Na], and decreased urine osmolality. These findings are consistent with a selective throttling of blood flow to the JMG during high Na feeding resulting in a relative decrease in JMGFR and medullary blood flow compared to low Na feeding. A localized increase in vascular and nephron volume is an alternative explanation.

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INTERACTION BETWEEN ADENOSINE COMPOUNDS AND NORADRENALINE IN THE RENAL CIRCULATION. K. Hashimoto. Dept. of Pharmacology, Tohoku Univ. Sch. of Med., Sendai, Japan.

Drugs were administered directly into the left renal artery which was perfused with heparinized own blood led from the femoral artery at a constant pressure in anesthetized dogs; the renal artery responded to a single injection of adenosine with prompt vasoconstriction, while initial vasoconstriction induced by infusion of adenosine recovered to the control level even though infusion was continued. In the higher rate adenosine was infused, the more rapid recovery to the control level was observed; (2) the vasoconstriction caused by a single injection of adenosine not only depressed but also converted to vasodilation during infusion of adenosine ('self-inhibition'), while noradrenaline-induced vasoconstriction was significantly enhanced even in the concentration of 0.3×10-9 g/ml. of adenosine. An increase in the infusion rate of adenosine made the enhancement more evident. The vasoconstriction caused by stimulation of renal periarterial nerve fibres was also significantly potentiated. Both selfinhibition of adenosine and potentiation of effects of noradrenaline and nerve stimulation disappeared promptly after interruption of adenosine infusion; (3) infusion of AMP acted similarly with that of adenosine but the effects were less potent. Infusion of ADP and ATP also depressed vasoconstrictor effect of adenosine while the effect of noradrenaline was less potentiated by ADP infusion and not by ATP infusion; (4) adenosine or AMP may probably modulate adrenergic mechanism in the renal circulation.

MULTISENSORY INPUTS TO PROJECTION AREAS OF LISSENCEPHALIC CORTEX.

J. Hassmannová, J. Mysliveček, J. Záhlava. Inst. of Pathophysiology,
Charles Univ. Med. Faculty, Plzen, Czechoslovakia.

Lissencephalic cortex has been considered as composed almost completely of projection areas. Our previous results showed that in a specific projection area of the rat neocortex evoked potentials (EP) can be obtained onto stimuli of another modality.

EP s to sound, light and electrical stimulation of forelegs in the somesthetic, auditory and visual cortical projection areas were registered by means of an average response method. Unit responses to these stimuli were taken, saved on a magnetic tape, and then analyzed by different kinds of time-interval and frequency histogramms. Our by different kinds of time-interval and frequency histogramms. Our results show that the primary cortical projection areas in the rat react to stimuli of other modalities by responses which have some characteristics typical for associative cortex.

701 STUDIES CONCERNING RENIN SECRETION REGULATION FACTORS ON ISOLATED AND PERFUSED KIDNEY IN DOGS; I.Haulică, D.Brănisteanu, Gh.Petrescu and Valeria Rosca. Dept.of Physiology, Faculty of Medicine, Jassy, ROMANIA.

The comparative study of plasma renin activity using the Helmar (1963) and Boucher (1966) techniques in dog isolated kidney perfused with autogenous blood, demonstrated that reduction of perfusion pressure to 30 mm Hg determined a rise in plasma renin activity; elevation of perfusion pressure in the isolated kidney induced in approximatively 66 % of the cases, a decrease in plasma renin activity, a phenomenon suppressed by novocaine; hyperosmosis caused by addition of 10% NaCl in the perfusion fluid, induced biphasic effects: initial rise of plasma renin activity followed by a subsequent decrease; hypoxia caused by bubbling the perfusion blood with 10-15% CO₂ determined activation of plasma renin. The data obtained seem to demonstrate that the rise in perfusion presum and in Na level brings about significant changes in plasma renin activity. A hypothesis is suggested for the reserpine-like action of harmonic resmosis on renin release.

702 CHANGES IN THE ACID-BASE STATUS OF THE BLOOD AFTER REPEATED MAXIMAL PERFORM-ANCE.V.Havel, O. Škranc. Dept. of Physiology, Med. Fac., Charles Univ., Hradec Králové, Czechoslovakia.

Six students 20 yrs old worked on a bicycle ergometer repeatedly at the performance of 450 w up to exhaustion at 5 min intervals until the impossibility of continuing work. The values of lactic acid pH, base excess, standard bicarbonate, $P_{0,2}$, $P_{C0,2}$ were determined by Astrup's micromethod. This type of loading led to a state of metabolic acidosis in the zone of compensation near the zone without compensation (pH 7.13, $P_{C0,2}$ 29 mm Hg, actual bicarbonate 11.5 or 7 mEq/1, lactic acid 16.4 m M/1). In the subject with greatest changes in the acid-base status another experiment was made with the same amount of work as before, but divided into 10 s intervals - followed by rest in the same proportion between work and rest as in the first experiment. In contrast to the first experiment in which the subject ended in exhaustion, in the present experiment the subject was fit and the whole performance was made in light hyperventilation alkalosis. We can conclude that a healthy subject can work with great acidosis of blood, without any sequels and that anaerobic processes predominate in this type of exercise. When the load is divided into short intervals the acid-base status is maintained without any changes and predomination of aerobic processes is supposed.

BRAIN ADRENERGIC SYSTEMS. V. Havlicek. Dept. of Physiology, Univ. of Manitoba, Winnipeg, Canada and Inst. of Higher Nervous Activity, Palacky's Univ., Olompuc, Czechoslovakia.

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The action of the ascending adrenergic system on higher centers of the brain appears to be predominantly inhibitory as increases in the brain norepinephrine (NE) content of rats induced by the administration of its precursor dl-3, 4-dihydroxyphenylserine (DOPS), are associated with augmented acoustically-evoked cortical potentials, a prolongation of the slow wave phase of sleep, a reduced period of EEG activation and decreased spontaneous and conditioned motor activity. Extracellular concentrations of glutamic acid in the cerebral cortex of DOPS treated rats are reduced and this may be related to alterations in cerebral activity. The peak of the NE induced inhibition occurs 4-6 hours after injection of DOPS and the muscular hypotonia and fatigue observed at this time may be a result of an increased efficacy of the descending adrenergic system. (Supported by Medical Research Council of Canada).

ACTIVITY OF SINGLE THALAMIC NEURONS IN THE MONKEY (MACACA MULATTA) DURING SLEEP AND WAKING. J.N. Hayward. Dept. Anatomy & Brain Res. Inst., UCLA School of Medicine, Los Angeles, Calif. 90024, U.S.A.

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Input from peripheral receptors and sleep-waking behavior influence the spontaneous firing patterns of single cells in the somesthetic thalamus of the moving monkey. Four adult female animals were prepared under pentobarbital anesthesia with cranial platforms, head-fixing bolts and skull cylinders positioned over the ventrobasal thalamus. An hydraulic microdrive and tungsten microelectrodes allowed stereotaxic exploration of the thalamus while behavior, body and eye movements, skin and nasal temperature and EEG were monitored. Some units found in the lateral portion of VB fire synchronously with the movements of breathing due to mechanical stimulation of their receptive fields. Other cells in the ventrobasal complex show increased discharges during movement due to natural stimulation of their cutaneous receptive fields. Most thalamic cells discharge spontaneously in bursts during slow sleep and at a faster, more regular pattern during waking, showing identical evoked bursts to mechanical stimulation during sleep and waking. In the waking animal certain cells in VPL show discharges to peripheral stimulation that cannot be obtained during the animal's slow sleep. These results suggest a convergence on ventrobasal thalamic neurons of specific, peripheral cutaneous input and non-specific 'central' input related to the level of sleep-wakefulness. (Supported in part by USPHS, NIH Grant NS-05638 and Special Fellowship NS-02277)

THE PHYSICAL STATE OF WATER IN CONTRACTILE TISSUE: AN NMR STUDY. C.F. Hazlewood, R.L. Vick, B.L. Nichols, and M.C. Harvey. Departments of Pediatrics and Physiology, Baylor College of Medicine, Texas Children's Hospital and Shell Development, Houston, Texas 77025, USA.

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Relative to that of free water, the motional freedom of water in skeletal and cardiac muscle is significantly reduced. Studies using high resolution nuclear magnetic resonance (NMR) spectroscopy show that the cellular water of skeletal and cardiac muscle must exist in one or more ordered states and that the free and the ordered water exchange rapidly. The usual NMR spectrum for free water is a narrow (1-2 Hertz) signal. Skeletal muscle of the rat, mouse, and dog yields broad NMR spectra (13-15 Hertz). Similar spectra are observed with various cardiac tissues of the dog and the rat. This broad spectrum obtained with muscle is an indication of orientation, adsorption, or ordering of water molecules. The following evidence favors the concept of substantial water orientation in skeletal muscle: (1) ions in high concentration did not broaden the water peak; (2) muscle with added free water produces a single peak which is narrower than that of muscle water and broader than that of free water; (3) denaturation of muscle protein results in a sharp, narrow water spectrum comparable with that of free water.

(Work supported by Texas Heart Association, Medical Research Foundation of Texas, R.A. Welch Foundation, U.S.P.H.S. Grants RR-00188, FR-05425, FR-00254, FR-00259, AM-011285, HE-08372, and 5-K3-HE-05421).

REGULATION OF BILE FORMATION IN SHEEP. T.J. Heath and I.W. Caple. Sch. of Physiology and Pharmacology, Univ. of New South Wales, Kensington, New South Wales 2033,

Australia.

The control of bile formation was studied in conscious sheep with bile fistulae.
The sheep were deprived of bile but received daily infusions of a salt solution into the duodenum to prevent electrolyte depletion. Sodium taurocholate was infused into the portal vein at 22 - 280 umole/min, and this stimulated the flow of bile and its content of bile salt anions and other ions, and of phospholipids. Secretin, infused content of bile salt anions and other ions, and 3.24 U./min also acted as a powerful into the portal vein at rates between 0.38 and 3.24 U./min also acted as a powerful choleretic. It is concluded that both recirculated bile salts and the hormone secretin could play a part in regulating bile formation in sheep.

This project was supported by grants from The Australian Wool Board and The George Aitken Pastoral Research Trust.

POSSIBLE ELECTROGENIC TRANSPORT MECHANISMS IN CARDIAC FIBERS. Hans H. HECHT & Masayasu HIRAOKA, Dept. of Med., Univ. of Chicago, Chicago, Ill., U.S.A.

Prolonged cooling of sheep Purkinje fibers stored for 24 hrs in 1mm-K+
Tyrode revealed changes on rewarming which are compatible with transport of
net charges across the cell membrane (electrogenic pump mechanism): Resting
membrane potentials (RMP) were recorded on rewarming to 37°C in 5.4mm-K+Tyrode solution up to 7 hrs after cold storage. Maximum RMP of 98.6mV+1.3 (S.
E.) were reached from 30-150 min after rewarming and declined to pre-cooling
levels after 5 hrs. The observed hyperpolarization was 18.8mV+1.8 (SE)
more negative than the mean RMP of uncooled fibers. The changes are noted
in high K (10.8mM) but are abolished in low K (2.7mM) solution. Pretreatment
with Ouabain (10-5M) before rewarming blocks hyperpolarization. Action
potential (A.P.) during hyperpolarization showed a less prominent overshoot
and plateau, and short AP duration. Marked positive after potentials were
noted during the period of hyperpolarization. Occasionally spontaneous
activity originating from oscillatory potentials occurred during recovery.
(Supported in part by Chicago Heart Assoc., USPHS grant HE-05673-06 and
PHS grant 43-68-1334.)

708 IMPORTANCE OF INTRACELLULAR SODIUM CONCENTRATION FOR SALIVARY SECRETION. J.Hedemark Poulsen. Inst. of Med. Physiology, Dept. A, Univ. of Copenhagen, Denmark.

When a salivary gland is stimulated to secrete, it looses potassium to the blood or perfusion fluid by a passive process (Burgen). The present experiments have demonstrated that this potassium loss is associated with the uptake of an equal quantity of sodium, also by a passive process. It is well known that an increased intracellular sodium concentration stimulates an active outwards sodium transport. It is therefore possible, that the passive sodium uptake stimulates an active sodium transport across the luminal cell membrane important for the formation of saliva. The finding that ouabain (10 4M) given intraductally is able to abolish the secretion supports this hypothesis. Burgen, A.S.V., J.Physiol. (1956). 132.20-39.

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EFFECTS OF CYCLIC AMP AND PROSTAGLANDINS ON ACTH SECRETION. G. A. Hedge. Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724, U.S.A. Cyclic AMP (cAMP), related substances, and several prostaglandins were tested for ACTH releasing activity by stereotaxically microinjecting them into the anterior pituitaries or basal hypothalami of anesthetized, dexamethasone pretreated female rats. Fluorometric determination of plasma corticosterone 15 min. after injection was used as an index of ACTH secretion. The dibutyryl analog of cAMP (5-50 μg) and theophylline (2-20 μg) were both found to cause ACTH secretion when injected into the pituitary, and the former does the same when injected into the basal hypothalamus. cAMP itself (6.5-65 μg) is effective only phylline. Both pituitary and hypothalamic responses to dibutyryl cAMP were diminished by high doses of corticosteroid. Prostaglandins E1, $F_{1\alpha}$, and $F_{2\alpha}$ (0.5-1 μg) had no effect on ACTH secretion when injected into the pituitary, but were very effective upon injection into the medial basal hypothalamus. The effects of these substances were decreased by high doses of dexamethasone, and abolished by morphine pretreatment. The responses to the prostaglandins were not augmented by theophylline pretreatment. All doses of all active substances were ineffective upon intravenous administration or injection into the lateral hypothalamus. Conclusion: cAMP may mediate the secretion of ACTH by acting at both hypothalamic and pituitary levels. The prostaglandins can indirectly cause ACTH secretion by acting at the hypothalamus. (Supported by USPHS; General Research Support and Research Grant AM 13794).

PLASMA INSULIN LEVEL AND INSULIN SENSITIVITY IN RATS WITH HYPOTHALAMIC DEAFFERENTATION. V.Hefco,P.Jitariu,P.Rotemberg.Dept.of Physiology,Univ."Al.I. Cuza",Yassy,Rumania.

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After medial hypothalamic deafferentation at frontal(FD), fronto-lateral (FL) or complete levels (CD), parallel with corticoadrenal hormone determination, sensitivity to insulin(IS) and plasma insulin level(PIL) were followed in rats too weeks post-operatively. There is an increased IS after FD and FL and decreased IS after CD. Mechanical interruption of nervous connections between ventromedial and ventrolateral nuclei do not lead to hyperphagia or changes in fasting blood glucose level. Addrenal hormone production progressivelly increased in order: FD, FL, CD. The degree of IS is attributed to the resultant action of growth hormone and corticoadrenal activity. Without denying the direct role of the central nervous system, our results point out a direct connection between plasma ACTH concentration and PIL and on the other hand that increased PIL is not due to hyperglycaemia.

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HYPERVENTILATION IN PATIENTS WITH CHRONIC HYPERCAPNIA. H.O. Heinemann, R.M. Goldring and G.M.Turino. Depts. of Medicine, Cornell, New York and Columbia Universities, New York, NY The critical variable determining renal bicarbonate (HCO3) excretion in patients with chronic hypercapnia undergoing mechanical hyperventilation is the reduced arterial PCO2. The roles of chloride (Cl), potassium (K) and sodium (Na) on HCO3 excretion during acute hyperventilation are not clearly defined. Bicarbonate divresis and urinary and extracellular electrolyte concentrations were studied during acute mechanical hyperventilation in four patients with chronic stable hypercapnia maintained on constant diets with "low" NaCl (20 mm/day) or "high" NaCl (>50 mm/day) content. On the day of study patients were hyperventilated in an Emerson body type respirator for 3-4 hours to lower arterial PCO2. Urine was collected during hyperventilation by spontaneous voiding. Supplements of KCl (40 to 60 mEq) were administered intravenously during mechanical ventilation. Results indicate that high NaCl intake and KCl supplements facilitated HCO3 diuresis. excretion on low Na intake was predominantly associated with K loss irrespective of KCl supplements; HCO3 excretion on high NaCl intake without KCl supplements was accompanied by Na diuresis. Addition of KCl intravenously to a high NaCl diet induced a marked HCO3 diuresis and increased both Na and K excretion. The rate of HCO3 excretion was related to change in $P_{\text{CO}2}$ induced by the respirator. However, NaCl and KCl affected this rate in that for a given change in $P_{\rm CO2}$ bicarbonate excretion was facilitated by a high NaCl intake and the administration of RCl supplements.

THE EFFECTS OF CHLORIDE, POTASSIUM AND SODIUM ON BICARBONATE EXCRETION DURING MECHANICAL

APPARENT INTRACELLULAR BUFFER VALUE OF SKELETAL MUSCLE AS RESULT-ANT OF CHEMICAL BUFFERING AND INTRACELLULAR-EXTRACELLULAR EX-CHANGE. N. Heisler and J. Piiper. Max Planck Inst. of Exptl. Med., Göttingen, Germany.

The intracellular buffer values derived from measurement of intracellular pH by the DMO method on the average are much lower than those obtained by titration or CO2 equilibration of muscle homogenates. The discrepancy could be due to intracellular-extracellular net exchange of bicarbonate ions (or to equivalent exchange of H or OH ions). This hypothesis was tested in rat diaphragms suspended in small volumes of Ringer solution equilibrated with 2% to 15% CO2. The mean effective intracellular buffer value obtained by the DMO method was 23 meq/pH per kg intracellular H2O, in agreement with most other studies. However, the pH changes in Ringer solution revealed that more than one half of the bicarbonate produced or disintegrated in cells in the course of buffering had been exchanged with the extracellular space. From the sum of intracellular concentration change and intracellular-extracellular exchange of bicarbonate, the true chemical buffer value was estimated at 86 meq/pH per kg intracellular H2O. According to this result intracellular-extracellular exchange is very significant in tissues buffering and must be taken into account when intracellular buffering is to be evaluated and interpreted.

713 INFLUENCE OF ION ALTERATIONS ON THE STRYCHNINE EFFECT ON APLYSIA NEURONS. W.-D. Heiss, M.R. Klee and D.S. Faber, Neurosensory Lab. and Lab. Neurobiol., Dept. Physiol., State Univ. of New York at Buffalo, Buffalo, N.Y., USA.

In 50% of Aplysia neurons in the visceral ganglion strychnine (o.1-1mM) in the bathing medium typically produces burst discharges, while in all cells investigated increased spike duration and slightly reduced resting potential, spike amplitude and positive afterpotentials result. Voltage clamp analysis of these effects showed an increased duration of the inward transient current and a reduction of the outward current. The changes observed in voltage recordings were enhanced by: i) Reduction or elimination of calcium, ii) addition of cobalt chloride (30mM), which is known to block competitively the calcium component of these spikes, and iii) addition of ouabain (o.3mM). Prolonged exposure to strychnine in combination with i) or ii) causes depolarizations of long duration and finally completely inactivates the spike generating mechanism. The strychnine effects were reduced by increasing calcium concentration 8-fold (88mM) and replacing sodium by Tris, the latter procedure blocking bursting only. Changes in potassium concentration, affecting the resting potential and spike parameters possibly by affecting the Na⁺/K⁺ pump, did not interfere with the bursting of cells. The effects of increasing calcium are comparable to the interaction of calcium with procaine and TTX, suggesting that strychnine induces bursting by altering calcium dependent sodium and potassium conductances changes.

714 EFFECT OF ACUTE AND CHRONIC HYPOXIA ON CARDIOVASCULAR REFLEXES IN MAN. D. D. Heistad, R. C. Wheeler, and A. L. Mark. U. S. Army Res. Inst. Environmental Medicine, Natick, Mass., and Univ. of Iowa Hosp. and V. A. Hosp., Iowa City, Iowa, U. S. A. Experiments were done to determine the effect of acute and prolonged hypoxia on reflex

Experiments were done to determine the effect of acute and prolonged hypoxia on reflex vasoconstriction. The response of forearm resistance vessels to lower body negative pressure (LBNP) was compared in 11 young men while breathing air and 12% oxygen during 2 sessions: a control session (acute hypoxia) and immediately after 36 hours in a hypobaric chamber at a barometric pressure of 446 mm Hg (equivalent to breathing 12% oxygen). Forearm blood flow was measured with a plethysmograph and arterial pressure by auscultation. In the control session the forearm vasoconstrictor response to LBNP was less while breathing 12% oxygen than while breathing air. Elimination of the hypocapnia during acute hypoxia did not restore responsiveness, indicating that decreased vasoconstriction during acute hypoxia is not due to the associated hypocapnia. After 36 hours of hypoxia, reduction in vasoconstrictor response continued while breathing 12% oxygen and vascular responses were promptly restored by breathing air. Measurement of the response of heart rate to LBNP suggested interference with cardiac, as well as vascular, reflexes during both acute and prolonged hypoxia. Vasoconstrictor responses of 2 chronically hypoxic patients have also been studied to determine whether adaptation of vascular reflexes occurs during chronic hypoxia. In both patients vascular responses to LBNP were depressed, and improved oxygenation (by breathing 100% oxygen) enhanced vasoconstrictor responses. These studies indicate that acute and prolonged hypoxia interfere with vasoconstrictor reflexes and correction of hypoxia restores vascular responsiveness.

THE EFFECT OF ACETYLSALICYLIC ACID ON THE TASTE RESPONSE OF THE RAT. Göran Hellekant. Dept. of Physiology, Veterinärhägskolan, 104 05 Stockholm 50, Sweden.

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The chorda tympani nerve of the rat mediates the response to taste stimulation of the anterior part of the tongue. Repeated stimulation elicits responses of approximately the same magnitude, if the stimulus is rinsed away between each application. Changes of the responses obtained can then be related to changes of the excitability of the taste receptors. This can be used to study the effect of a substance on the sensitivity of a peripheral receptor. The study to be presented will show that local application to the tongue as well as parenteral administration (100 mg/kg body weight) of acetylsalicylic acid can diminish the taste sensitivity. This indicates that the analgesia of salicylates partly may depend upon their depression of peripheral receptors.

INTRARUNAL DISTRIBUTION OF BLOOD FLOW DEFERMINED WITH 133Xe IN THE RAT. J.Heller, J.Kasalický, Inst.Cardiovasc. Res., Prague, Czechoslovakia.

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An attempt was made to measure renal blood flow in anaesthetized rats An attempt was made to measure renal blood flow in anaesthetized rats using a washout curve of 133-Ae. The left kidne, was placed in a plastic dish for micropuncture and continually washed with liquid paraffin. A needle was introduced into the aorta cranial to the renal arteries for injecting 133-Ae, 70 µC in 0.05 ml isotonic saline. The radioactivity was detected by means of NaI crystalls and recorded with time constant of 0.5 sec. There were 4 components to the washout curve. In the range of arterial pressure 100 - 120 mmHg values were as follows (ml.(100g tissue weight.min) 1): Component I: 947 ± 97.1; comp. II: 164.8 ± 9.9; comp. III 24.6 ± 2.9; comp. IV: 34.4 ± 2.8. Comp. I was far higher than analogous values from similar experiments in dogs; comp. II was also somewhat higher. Comp. I values showed a high degree of scatter, the average value, however, was in good agreement with PAH clearance measured at the same her. Comp. I values showed a high degree of scatter, the average value, however, was in good agreement with PAH clearance measured at the same time, corrected for haematocrit (46 ± 2) which gave a value of 1006.1 ml.(100g.min) -. Comp. I, which probably represents cortical blood flow, requires only 5 - 6 min for measurement, so that repeated estimations may be made without interferring with a micropuncture experiment.

THE POSSIBLE CONTRIBUTION OF AN ABNORMAL RENSHAW INHIBITION TO EXTRAPYRAMIDAL RIGIDITY. H.-D. Henatsch and J. Meyer-Lohmann. Dept. of Physiology, II, Univ. of Goettingen, Goettingen, German Fed. Rep.

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An abnormal recurrent Renshaw inhibition at the spinal level might well be responsible for some symptoms of extrapyramidal disorders, particularly for the retarded and viscous type of movements and the cogwheel rigidity. This syndrome seems to result from an imbalance of central cholinergic and monoaminergic neuronal mechanisms. The Renshaw feedback itself is cholinergic at its first synapse, and anticholinergic agents are well known to relieve the rigidity to some extent. Imipramine which blocks re-uptake of noradrenaline and of 5-Hydroxytryptamine, but not of dopamine, at monoaminergic neuronal endings, can markedly suppress the spinal Renshaw inhibition (1). This drug is successfully used to improve modern L-DOPA treatment of Parkinson patients. The results of Meyer-Lohmann et al., presented elsewhere at this congress (2), further support the view that mono-aminergic supraspinal (dopaminergic?) and/or spinal (tryptaminergic?) influences affect the inhibitory Renshaw mechanism. While dopamine exhaustion might play the key role for the central (nigro-neostriatal) monoaminergic disturbance, we assume that some other monoaminergic action upon the spinal Renshaw inhibition is required in order to prevent extrapyramidal rigidity.
(1) U. Tan a. H.D. Henatsch; Naunyn-Schmiedebergs Arch, Pharmak.exp. Path. 262, 337(1969)
(2) J. Meyer-Lohmann et al.: This congress (abstract) (1971)

718 FIRING PATTERNS OF OCULOMOTOR UNITS IN THE GOLDFISH. H. T. Hermann, Neurophysiology Laboratory, McLean Hospital, Belmont, Massachusetts, U.S.A.

Simultaneous recordings, in the dark, of eye position and single unit nerve pulses in the mesencephalic tegmentum of goldfish revealed units well correlated with eye position and eye movement. The most frequently encountered units showed sustained nerve pulse rates proportional to eye position with zero rates at one extreme position and maximum at the other. As the eye saccaded in the direction correlated with increased nerve pulse rate, a short (~40 msec) burst of high frequency pulses initiated the change in pulse rate; no bursts occurred with saccades in the direction of the zero firing rate position. Other units correlated with saccadic motion of one direction only. A few units (not illustrated) showed steady high frequency firing rates with pauses during saccadic motion. None showed response to retinal stimulation. Removal of proprioceptor afferent nerve signals via dissection of extrinsic eye muscles did not affect the gross stepwise shifts in single unit firing rates. It did alter the pulse rate 'envelope' and the statistics of nerve pulse intervals. Also, the nystagmoid envelope of pulse rates induced by D. C. stimulation of vestibules was altered subtly by removal of proprioceptor feedback, but not in gross character oscillations.

719 RELATIONSHIP BETWEEN MAXIMAL OXYGEN UPTAKE AND HEMATOLOGICAL PARAMETERS. Lars Hermansen and Odd D. Vellar, Institute of Work Physiology, Oslo and Institute of Hygiene, University of Oslo, Oslo, Norway.

The relationship between maximal oxygen uptake and different hematological parameters has been investigated in 72 school-children (boys and girls) and 97 trained students (males and females). Maximal oxygen uptake was estimated either by measurement of oxygen uptake during maximal treadmill exercise (direct method) or calculated from measurements of heart rate during submaximal bicycle exercise (indirect method), or both. Hemoglobin concentration (Hb), hematocrit (Hct) and mean corpuscular hemoglobin concentration (MCHC) were measured in all subjects. In addition, serum iron, total iron binding capacity (TIBC), transferrin (sat. %) and the total quantity of hemoglobin (THb), were measured in a sampling of male and female students. Correlation analysis revealed a highly significant positive relationship between maximal oxygen uptake (liter/min) and Hb, Hct and THb in the total material. However, when the total material was divided into subgroups (school-girls, school-boys, female or male students), or when maximal oxygen uptake was corrected for differences in body size (ml/kg x min), no consistent relationship could be demonstrated. Furthermore, no consistent relationship could be demonstrated. Furthermore, no consistent relationship could be demonstrated between maximal oxygen uptake (liter/min or ml/kg x min) and MCHC, serum iron, TIBC and transferrin (sat. %) neither in the total material examined, nor in the different groups.

720 MECHANISM OF FORMATION OF AMMONIUM BICARBONATE BY THE CROCODILIAN KIDNEY. THOMAS
HERNANDEZ AND ROLAND A. COULSON, Departments of Pharmacology and Biochemistry, Louisiana
State University Medical Center, New Orleans, Louisiana 70112.

The main end product of nitrogen metabolism in the crocodilian is ammonium bicarbonate which ordinarily accounts for 2/3 of the osomotic pressure of the urine. The urine is alkaline (ph 7.8) and practically free of NaCl. The injection of glycine, alanine, or glutamine causes great increases of both NH3 and HCO3. Carbon-14 labelled amino acids produced ammonium bicarbonate with high specific activity in bicarbonate. The presence of NH4HCO3 in an alkaline urine cannot be explained solely by the diffusion of NH3 into an acid urine. Formation of carbamyl phosphate from NH3, CO2 and ATP with carbonic anhydrase as a catalyst could explain the diffusion of equal amounts of ammonia and CO2 into the urine. Carbamyl phosphate appears to diffuse into the lumen and then in the absence of carbonic anhydrase in the lumen, NH4HCO3 is formed spontaneously. If carbonic anhydrase is inhibited by acetazoleamide, carbamyl phosphate cannot be formed. Chloride which is ordinarily reabsorbed after bicarbonate formation remains in the tubule creating an acid media for the trapping of the ammonia. The mammal may be like the crocodilian in ammonia formation. If an ammonia precursor is infused in the dog, the urine becomes alkaline and rich in NH3. The formation and diffusion of carbamyl phosphate into the tubule could explain the occurrence of ammonia in the alkaline urine of certain mammals.

SEASONAL AND DIETARY INFLUENCES ON THYROXINE SECRETION RATE IN WHITE RATS KEPT OUTDOORS. O. Héroux and M. Jobin . Natl. Res. Council of Canada, Ottawa, Ont., Faculty of Med., Laval Univ., Quebec, P.Q., Canada.

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Thyroid secretion rate (TSR) was estimated from thyroxine (T_4) turnover rate values by using the single injection isotope dilution technique in male Sprague Dawley rats. Three groups of 28 rats of an average body weight of 230 g were moved outdoors either in Spring, Summer, or Winter. The animals were kept in groups of 15 in large cages, on shavings; half were fed Master Lab cubes (MLC) and tap water ad libitum whereas the other half received a semi-purified diet (T_4 F) in pellet form and a 0.12 mg/100 ml KI drinking solution ad libitum. Independently of the diet, a) Winter metabolic clearance rate (MCR) of T_4 was significantly faster than in Summer, and essentially the same as in Spring, b) T_4 blood level in Winter was significantly lower than in Summer and the same as in Spring, c) the product of the two revealed no significant difference in TSR between the three seasons. Independently of the season, rats on T_4 F showed a) a blood T_4 level significantly higher than rats on MLC, b) an MCR which tended to be lower, c) a TSR which was essentially the same as in the MLC group. In conclusion, contrary to lab cold temperature acclimation, outdoor winter acclimatization does not result in an increased TSR, and the only significant influence of diet was on the higher blood T_4 level in T_4 F rats than in MLC rats.

STEADY STATE OF REGULATING METABOLITES IN WEANING RATS. E.Herrera, A. Aranda and E. Blázquez. Inst. G. Marañón, C.S.I.C., Madrid-6, Spain.

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We have studied the steady state levels of regulating metabolites when the diet of weaning rats changes progressively from the mother's milk(low-carbohydrate but high-fat and high-protein) to standard solid diet and compared them with those of adults(A). When fed, 5 and 10 days old rats present normal glycemia(g) and high ketonemia(k) and normal liver citrate(c) and acetyl-CoA(aC), high lactate/pyruvate ratio(1/p) and FFA and low glycogen(G). 20 days old rats present normal g,k,c,aC,1/p and G and high FFA. After a 24 h fast, 5 and 10 days old rats show high g,k,c and FFA, low aC and normal I/p and G. 20 days old rats have high g,k,c,FFA and G and low aC and 1/p. At 30 days of age the differences with A are less but g,k,FFA and G are high and aC and 1/p low. Conclusions: Soon after birth the high lipid content of the milk permits maintainance of such steady levels of regulating metabolites in the liver that gluconeogenesis is enhanced and lipogenesis inhibited. At 20 days, when the intake in carbohydrate rises(pellets), the high ketonemia, combined with the observed changes in other metabolites, allows maximal storage capacity of glucose as glycogen. The high lipid availability allows the newborn animals to preserve fasting glycemia better than adults. (Supported by The Wellcome Trust, London).

INHIBITION OF SODIUM TRANSPORT IN TOAD BLADDER BY ETHACRYNIC ACID. <u>Francisco</u> <u>C. Herrera</u>. Departamento de Ecología, IVIC, Caracas, Venezuela. Supported in part by a grant from Fundación Vargas.

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In toad bladder ethacrynic acid (EA) decreases short-circuit current (SCC) from 185 $\mu Eq/hxg$ dry weight (d.w.) in controls to 23 $\mu Eq/hxg$ d.w. in bladders treated with 1 mM EA. Mucosal to serosal (MS) Na flux fell from 193 $\mu Eq/hxg$ d.w. to 92 $\mu Eq/hxg$ d.w. after EA. The decrease in SCC is greater than that of MS Na flux. Potential difference fell to 0 mV at the end of the exposure to EA; in controls it remained at 45 mV. Tissue Na was 374 $\mu Eq/g$ d.w. in controls and 464 $\mu Eq/g$ d.w. in bladders exposed to EA. Tissue K was 220 $\mu Eq/g$ d.w. in controls and 164 $\mu Eq/g$ d.w. after EA. The effects of EA were significant at or below P < 0.01 level. The difference between the tissue spaces accessible to mucosal Na-22, 50 $\mu Eq/g$ d.w. in controls and 72 $\mu Eq/g$ d.w. after EA, was not statistically significant. The effects of EA on SCC and MS Na flux suggest that it acts on the overall transport of sodium across the epithelium. It does not decrease intraepithelial sodium space indicating that it acts on the sodium pump rather than on the Na permeability of the apical cell border. The increase in tissue Na is probably due to serosal sodium. The high MS Na flux after EA and the discrepancy between the decrease in SCC and MS Na flux caused by EA suggest the existence of a large passive shunt in bladders treated with EA.

724 SOME EFFECTS OF ALLOXAN UPON THE EHRLICH ASCITES CELLS, IN VITRO.

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Romania.

Alloxan added to the suspension of Ehrlich ascites cells induces an important mortality, which can be demonstrated by the trypan blue staining procedure. Swiss mice having received intraperitoneally Ehrlich ascitic cells incubated with alloxan o,1 M.at 37°C for an hour, presented a more prolonged evolution of the ascitic tumor and alonger duration of survival as compared with the controls. Oxygen consumption by cells, measured manometrically by the method of Warburg (in the presence of o,o1 M.alloxan), did show a very great increase in the first 15 minutes, which generally was followed by an subsequent inhibition.

725 CAUDAL BRAIN STEM STRUCTURES MEDIATING THE PRECIPITATED MORPHINE ABSTINENCE SYNDROME A. Herz, Hj. Teschemacher, K. Albus a. S. Zieglgänsberger; Max-Planck-Inst. für Psychiatrie, Munchen, Germany. In rabbits tolerance and drug dependence were induced by injection of increasing doses of morphine; then an abstinence syndrome was precipitated by application of morphine-antagonists. The animal's behaviour was observed, body temperature, heart frequency and respiration were registered. The abstinence syndrome provoked by intracerebroventricular application of antagonists was similar to that provoked after systemic application; yet, with intraventricular application smaller doses were effective and the syndrome was generally more pronounced. Only a few symptoms present after systemic application of antagonists could not be observed after intraventricular application. With smaller doses of antagonists the syndrome was dominated by a characteristic motor excitation, with higher doses convulsive sympotoms became prominent. Application of nalorphine into separated parts of the ventricular system (VS) allowed a further differentiation of sites of action. From the anterior part of the VS (including the lateral ventricles and third ventricle) no or only weak symptoms could be evoked; a very vigorous abstinence syndrome was precipitated by application of nalorphine into the fourth ventricle, however. From this is concluded, that structures in the caudal brain stem, most probably in the floor of the fourth ventricle are important substrates for the development of drug dependence on morphine. The site of action for the inhibition of nociceptive reactions was also found to be situated in this area, (HERZ et al., Neuropharmacol. 9, 539 (1970)).

THE ANALYSIS AND COMPUTER SIMULATION OF THE FEEDBACK BETWEEN THE RATES OF GLUCOSE PRODUCTION AND UTILIZATION AND PLASMA GLUCOSE CONCENTRATION IN DOGS.

G. Hetenyi Jr. and K.H. Norwich Dept. of Physiology, U. of Ottawa and Inst. of BioMedical Electronics, U. of Toronto, Canada.

Experiments were carried out on trained conscious dogs. Each dog was

Experiments were carried out on trained conscious dogs. Each dog was subjected to 4 or 5 experiments. In each experiment glucose has been infused i.v. at a constant rate. This rate was varied between the different experiments on the same dog. During such infusions (step functions) plasma glucose levels rose and after passing a peak at 25-40 minutes after the start, settled at a constant level (\bar{c}) between 85-185 mgg. In these steady states, rates of glucose utilization (Rd) were calculated by a tracer method with Cl4-1-glucose as the tracer. Plotting Rd against \bar{c} an excellent straight line fit was obtained within the range studied. The plot of Ra_vs \bar{c} appeared to be compatible with the function of Ra=Ra (max). (exp. λ . \bar{c}) + K._ These equations predicted the shape of the plot: rate of infusion vs. \bar{c} . A digital computer model based on these equations accurately predicted the changes of plasma glucose levels both after an i.v. injection or during an infusion of glucose. Some parameters of the model depend on the release of insulin. (Supported by the MRC of Canada).

STIMULATION OF FISH CHEMORECEPTORS BY MIXED SOLUTIONS OF ACID AND SALT. I. Hidaka, Faculty of Fisheries, Mie Prefectural University, Tsu, Mie Prefecture, Japan.

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Fresh-water fishes including the carp have comparatively a high sensitiveness to acids. It was attempted in the present study to examine the effects on the acid receptor of neutral salts applied in acid solutions by recording the response from the palatine nerve supplying the palatal chemoreceptors of the carp. Addition of NaCl to HCl solutions resulted in an enhancement of the multifibre summated response: The mixture of 0.001 M HCl with 0.002 M NaCl, for example, elicited a response larger in magnitude than the algebraic sum of those for the single HCl and NaCl solutions. The enhancement increased with increasing NaCl concentration below 0.05 M; above 0.05 M the rate of rise of the enhancing effectiveness declined gradually with increasing concentration. The enhancement was prominent at low HCl concentrations (0.0005 to 0.0025 M); above 0.0025 M it declined gradually with increasing concentration ; and no marked difference in response magnitude was noted between 0.01 M HCl and the mixture containing 0.01 M HCl and 0.05 M NaCl. Similar enhancements were observed with several chloride salts having different monovalent or divalent cations and sodium salts of different monovalent anions. Experiments with single fibre were carried out. Fibres were found which did not respond to NaCl but responded to its mixed solutions with HCl of various concentrations in spike frequencies higher than those noted in responses to the single HCl solutions. Thus the results suggest that the enhancement of the response by NaCl may be related to the activity of the acid receptor rather than the salt receptor.

SYNAPTIC LINKAGE FROM THE Y GROUP OF THE VESTIBULAR NUCLEI TO THE OCULOMOTOR NUCLEUS IN RABBIT S.M. Highstein Department of Physiology University of Tokyo, Japan

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The Y group of the vestibular nuclei was stimulated by using a fine glass pipette electrode and the effect was examined in the oculomotor nuclear complex utilizing intracellular recording techniques. It was thus revealed that Y group stimulation evoked monosynaptic excitatory postsynaptic potentials(EPSPs), range of latencies 0.5 to 1.2 milliseconds, in those motorneurons innervating the contralateral inferior oblique and ipsilateral superior oblique extraocular eye muscles. The oculomotor neurons innervating these muscles were identified by antidromic action potentials evoked by stimulating nerve branches to these muscles in the orbits. These EPSPs occluded with those evoked disynaptically by stimulating the whole eighth nerve, indicating that the Y group contributes at least in part to the disynaptic vestibulo-ocular excitation. Since the Y group receives afferent input from the saccule (Gacek 1969) and the saccule has been shown to contribute to ocular counter-rolling(Jongkees 1950) the possibility can be pointed out that the Y group, at least partially, mediates this portion of the tonic labyrinthine reflex to the eyes.

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A SCREENING PROCEDURE FOR NEUROTRANSMITTERS - ACETYLCHOLINE IN THE LOBSTER NERVOUS SYSTEM John G. Hildebrand, David L. Barker, Edward A. Kravitz, Department of Neurobiology, Harvard Medical School, Boston, Massachusetts 02115, USA

The identification of the neurotransmitter substance liberated at a particular synapse would be aided by a rapid screening procedure which tentatively identified transmitter candidates. We have developed such a method, based upon the selective synthesis and localization of transmitters in those cells which release them. The procedural steps are: (1) incubation of nervous tissue explants in a physiological medium containing radiochemical precursors of suspected transmitters (choline for acetylcholine, glutamate for GABA, tyrosine for catecholamines and tyramines, and tryptophan for serotonin); (2) isolation of radioactive nervous elements by dissection, followed by acidic extraction; (3) high-voltage paper electrophoresis of the extract under conditions which separate most of the compounds of interest; and (4) quantification of isotope incorporated into possible neurotransmitters. Using several preparations whose transmitters are known, the method has been tested and its effectiveness and sensitivity down to the single cell level, shown. In addition, it has been used in our continuing biochemical studies of synaptic transmission in the lobster, Homarus americanus. Particular attention has been addressed to identification of the transmitter employed by sensory neurons. Studies of single cells have yielded evidence, which will be presented, that acetylcholine may be the sensory transmitter.

730 PLACENTAL TRANSFER AND FOETAL METABOLISM, AND THE HIGH PLASMA FREE AMINO-ACID CONCENTRATIONS.
P. M. M. Hill and M. Young. Dept. Gynec., St. Thomas's Hosp. Med. Schl. London, England.

The high levek of all the free amino acids in foetal plasma relative to maternal, at all gestational ages, suggests greater net transfer from mother to foetus than foetal utilization. This transfer was studied in the near term foetal guinea-pig placenta perfused 'in situ' (Reynolds + Young 1971), with varying concentrations of amino acids. On open circuit, total ∝ amino No transfer decreased proportionally with the concentration in the foetal placental perfusion fluid. The A-V differences were small at concentrations equivalent to foetal plasma (6-8 mM) and thereafter no net transfer occured but, during closed circuit perfusion, concentrations of 13-18 mM were maintained for 60-90 minutes. Analysis of the individual amino acids showed that they are transferred across the placental barrier in the same proportion as they are present in the maternal plasma, with the exception of the branched chain amino acids which are transferred in relatively greater proportion. Naturally occurring umbilical vein artery differences are small and demonstrate transfer of the branched chain and basic amino acids from mother to foetus, but the production of glycine and taurine by the foetus (Young + Prenton 1969). The present results suggest that these small V-A differences are partially determined by the high free amino acid concentrations in the foetal plasma. The composition of the free amino acids in placental parenchyma will be reported. Part of the work was supported by the British Nutrition Foundation.

731 RHEOLOGICAL COMPARISON OF LUNG TISSUE AND LUNG LIMING. J.Hildebrandt, T. Horie, T. Sugihara, H. Bachofen and C.J. Martin. Virginia Mason Res Ctr, Seattle, Wash., USA.

The tissue component of the lung's elastic recoil is defined either by pressure-volume curves of saline-filled lungs,or by force-length curves of parenchymal strips. The contribution of the lung surface lining to recoil can be deduced from the pressure difference between saline and air curves. In this way the mechanical behavior of lining has been compared with that of tissue. (a) The magnitude of stress adaptation in air-filled lung is about 8 times that seen in the saline counterpart, but the direction of pressure change is the same. (b) Dynamic changes of lung compliance were also about 8 times greater with air. (c) Areas of hysteresis loops for tidal volumes (Vr) between 10% and 30% TLC in air are about 5 times those obtained with saline. In both, however, area is independent of frequency of cycling. In tissue strips 28% of the work of loading is lost as heat in each cycle, independent of cycling rate. (d) In air and saline-filled lung the hysteresis area can be expressed as A=KVTAP, where AP is the pressure amplitude, for VT up to 30% TLC. The value of K is about 11%. The foregoing rheological similarities might imply that mechanisms responsible for frictional losses in soft tissue are also important in producing hysteresis in the lining. None of these mechanisms is understood. There appear to be some differences between the properties of surfactant in vitro and those seen in situ, perhaps related to extraction procedure or to the nature of the subphases.

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732 CONVEYANCE OF URINARY AMMONIA TO MAMMALIAN KIDNEY AS BLOOD GLUTAMINE. A.G. Hills, W.D. Kerr, and E.L. Reid. Dept. of Med., Univ. of Miami School of Med., Miami, Fla., U.S.A.

The chief immediate source of the urinary ammonia is amine- and especially amide-N of Lglutamine conveyed to the kidney via the renal artery (Stone et al., 1967). Data are presented (1) to show that a substantial portion of net glutamine extracted by the kidneys is provided by glutamine release from peripheral tissues; and (2) to suggest that peripheral glutamine release represents removal from the peripheral cells of ammonia formed as the end-product of their protein metabolism. (1) In 12 greyhounds and 21 mongrel dogs fasted overnight, hindleg net glutamine output was consistently observed and averaged respectively .230 and .096 µmol/min/kg body wt (p < .001). Net glutamine output was estimated as the product of plasma venous-arterial glutamine difference and plasma flow calculated from blood flow (magnetic meter) and hematocrit. Net outflow of glutamine-N could not be accounted for as ammonia uptake. Findings in the spider monkey Paniscus ateles were similar. (2) Femoral arterial infusion of an ammonia salt consistently enhanced net glutamine output by the leg; the increase averaged .220 and .178 µmol/min/kg in 6 greyhounds and 14 mongrels respectively (p < .025). Increased glutamine output during ammonia infusion is interpreted as reflecting glutamine synthetase activity in peripheral tissues, probably chiefly skeletal muscle. Brain and probably other tissues also contribute to circulating glutamine; the system serves 2 functions at the supracellular level of organization: (1) provision of much of the urinary buffer ammonia for excess protons, and (2) defense against ammonemia.

ANTIBIOTICS AS TOOLS IN THE STUDY OF THE ROLE OF BROWN ADIPOSE TISSUE IN COLD-ACCLIMATION Jean Himms-Hagen, Dept. of Biochemistry, University of Ottawa, Ottawa 2, Canada.

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The aim of these experiments was to depress the metabolic activity of the brown adipose tissue (BAT) in intact rats during acclimation to cold in order to elucidate the possible thermogenic and endocrine functions of this tissue. In an attempt to inhibit the proliferation of mitochondria and of mitochondrial inner membrane known to occur in BAT in response to cold the antibiotic oxytetracycline (OTC) was administered twice daily for 2 weeks to rats living at 4°C; control rats received saline. Cytochrome oxidase (COX) served as an index of the amount of mitochondrial inner membrane of total BAT, liver and muscle. Development of an enhanced calorigenic response to noradrenaline served as a measure of the extent of cold-acclimation. Treatment with OTC inhibited both the cold-induced increase in COX in total BAT and the cold-induced development of an enhanced calorigenic response to noradrenaline. There was a direct correlation between the amount of COX in BAT and the size of the calorigenic response to noradrenaline; however, the amount of COX was itself too small to account for the extra oxygen consumed. Treatment with OTC did not alter the cold-induced growth of BAT (increase in wet weight and in total protein): neither did it alter COX in liver or muscle. The effect of OTC is fairly specific for the mitochondria of the most rapidly proliferating tissue, the BAT. The conclusion is drawn that a protein synthesized in the mitochondria of the brown adipose tissue is essential for adaptation to cold.

EFFECTS OF ENDOTOXIN ON MYOCARDIAL HEMODYNAMICS, PERFORMANCE, AND METABOLISM.

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Ctr., Oklahoma City, Oklahoma, U.S.A.

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The effect of endotoxin on the heart is obscure and results have been controversial. The purpose of the present study was to determine the effects of lethal endotoxin shock on myocardial hemodynamics, performance, and metabolism. Studies were carried out on an isolated working left ventricle removed from a donor dog exchanging blood with an intact support animal. Aortic pressure and cardiac output of the heart were decreased by pump adjustment to match the support animal's mean systemic pressure after endotoxin. Results indicate that endotoxin has no direct detrimental effect on the heart during a three-hour period of shock. Left ventricular end diastolic pressure, myocardial contractility, cardiac power (work/sec.) dP/dT, O2 uptake and CO2 production were 'statistically unaltered from initial control values in the face of severe systemic hypotension and acidosis in the support animal. Myocardial hemodynamics demonstrated marked increased coronary blood flow and loss of autoregulation after endotoxin. In summary, results exclude a direct cardiotoxic action of endotoxin, demonstrate a strong resistance of the myocardium in endotoxin shock and suggest that myocardial failure may occur only after extensively prolonged systemic hypotension. (Research supported by V.A. Hospital, U.S. Navy Project N00014-68-A-0496, and USPHS Grant HE 12302).

ELECTROPHYSIOLOGICAL CHANGES INDUCED BY COLD ON CARDIAC PURKINJE FIBERS.

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Changes in resting and action potentials on rapid or stepwise cooling were tested on cardiac Purkinje fibers. Multiple impalements and voltage clamp techniques in short segment of fibers were also used. Fibers were cooled from 37° to 4°C for 2 min to several hours. A rapid decrease in resting potential (RMP) on cooling exceeded the Nernst equation and remained steady from 2 to 30 min. (-41.2mV+5.69 S.E. and -36.7mV+5.02 S.E. RMP respectively. 2 hr cooling caused additional depolarization to -15.4mV+1.24 RMP. A Na+ dependent hysteresis like response was noted on cooling and rewarming and this rapid response was partially blocked in low Na+, low K+ and following Ouabain. Action potentials (AP) showed a transient increase in overshoot on cooling with a decrease of dv/dt. Excitability was lost and returned at a temperature threshold of about 23°C. On prolonged cooling excitability returned with a short AP duration. Membrane conductance and delayed rectification decreased markedly during cold exposure. Changes in membrane conductance and block of active transport mechanisms are implicated. (Supported in part by Chicago Heart Asso., USPHS grant HE-05673-06, PHS 43-68-1334.)

736 LACTIC ACID PERMEATION ACROSS SKELETAL MUSCLE CELL MEMBRANE. Hj. Hirche,
H.D. Langohr, U. Wacker. Inst. of Physiology, Univ. of Duesseldorf, German Fed. Rep.

Lactic acid (LA) permeation across muscle cell membrane was investigated in isolated, blood perfused, electrically stimulated gastrocnemii of the dog. Since LA permeation was much more slowly than LA formation during the phase of oxygen debt LA was accumulated at the beginning of work. The rate of LA permeation was not linearly proportional to the intracellular LA concentration but reached a saturation value. At low extracellular LA concentration and the rate of LA permeation could formally be described in terms of the Michaelis-Menten equation with a Km of 8.3 µmoles/g wet weight and a V max of 1.9 µmoles/g x min. That means that LA permeation out of the skeletal muscle cell is not a free but a facilitated diffusion. It could be calculated that the LA accumulation within the skeletal muscle cell prevents the organism from severe metabolic acidosis during the phase of oxygen debt or during exercise under hypoxic conditions. This view was further supported by the observation that V max of LA output decreased when the extracellular concentration of LA or H was increased.

737 MONOAMINES AND ACTIVITY REGULATION IN THE FRESH-WATER MUSSEL. L. Hiripi and J. Salánki. Biol. Res. Inst. Hung. Acad. Sci., Tihany, Hungary.

Quantitative changes of monoamines were investigated in the CNS of the fresh water mussel in connection with the periodicity of activity and rest. The synthesis and breakdown of serotonin and catecholamines were examined both in the brain and outside of the ganglia. According to the results, the changes of monoamine level are correlated to the alternation of activity and rest. The periodicity of the synthesis and / or storage of monoamines may lie in the basis of activity regulation. In the metabolism of monoamines the role of 5 HTP-DOPA decarboxylase and MAO were demonstrated. The synthesis takes place only within the CNS while MAO activity was found in extraneuronal tissues too. Depletion of monoamines from the neurones causes characteristic changes in the activity regulation of the animal.

DELAYED RESPONSE OF THE HYPOTHALAMO-PITUITARY AXIS TO STRESS DURING STRESS-NONRESPONSIVE PERIOD IN NEONATAL RATS. T. Hiroshige. Department of Physiology, Hokkaido University School of Medicine, Sapporo, Japan

Although the existence of the stress nonresponsive (SNR) period is claimed in the neonatal rat, no study has been made of the mode of participation of the hypothalamic CRF (corticotropin-releasing factor) in this process. Attempts were made in this study to know patterns of dynamic change of the hypothalamic CRF content in 2nd day rat neonates. CRF activity was assayed by our direct intrapituitary microinjection method. Stress used was exposure to ether vapor followed by laparotomy. In the initial 20 min period of observation, neither CRF content nor plasma corticosterone (B) levels were found to increase. This finding is in marked contrast to response patterns in adult rats and supports the existence of SNR period in the early postnatal days. After 40 min of observation, however, CRF content in the median eminence showed a significant increase, whereas plasma B level remained still low. In the next 20 min, plasma B also showed a similar increment. Even in the continuation of the stress, the elevated CRF level finally started to decrease 100 min after the start of stress, followed by a decline of plasma B level. The results indicate that SNR period is not absolute but responses to stress are merely delayed in this period. Furthermore, it is suggested that the change of CRF content is closely related to that of plasma B, the former always preceding the latter.

(Supported by a grant from the Ministry of Education of Japan)

DOSE RESPONSE STUDIES OF ATROPINE INHIBITION OF HISTAMINE- AND PENTAGASTRIN-STIMULATED GASTRIC SECRETION IN THE DOG. B. I. Hirschowitz and G. Sachs. Div. Gastroenterology, Dept. Medicine, Univ. of Alabama in Birmingham, Birmingham, Alabama, USA.

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In a group of 5 dogs, volume H⁺, Cl⁻, Na⁺, K⁺ and pepsin were measured in 18 x 15 min samples of gastric juice stimulated by continuous 4 hr 1.V. infusion of histamine (7 doses, 2-125 µg base/kg-hr, each dose in a separate exp.). At another time each dose was infused against a background of atropine sulfate (10 µg/kg-hr). Output of water and the dose-responsive secretion of each ion could be described by Michaelis-Menten kinetics, giving calculated values for threshold, S₅₀ and V^{max}. By a kinetic analysis of the dose response of (a) concentration and (b) output to histamine two types of histamine effect could be described, depending on the parameter analyzed: (a) When concentration is used as the response of the system, no threshold and a very low S₅₀ (< 1 µg/kg-hr) is observed. Atropine has no effect on these kinetics. (b) When output is used as the response, then the histamine threshold value is 2.5 µg/kg-hr, and the S₅₀ is 10 µg/kg-hr. Atropine competitively inhibits this process by increasing the S₅₀ to above 30 µg/kg-hr, leaving an unchanged V^{max}. In another group of 5 dogs given pentagastrin infusions (8 doses, 0.1 to 6.0 µg/kg-hr), kinetic analyses also show distinct differences when either concentration or output are used as the dose-responsive parameters. In this case, however, atropine acts as a strong inhibitor of both processes. This suggests significant differences between actions of histamine and pentagastrin on secretion.

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HISTAMINE RELEASE FROM HUMAN LUNG BY 48/80 AND METHYL PIPERONYLATE. M. Hitchcock, D.M. Piscitelli, and A. Bouhuys. J.B. Pierce Foundation Lab. and Yale Univ. School of Med., New Haven, Connecticut 06519, U.S.A.

Inhalation of cotton dust causes acute bronchoconstriction which may be due in part to non-allergic release of histamine (H). Inhalation of an aerosol of a tyrode soluble extract of cotton bracts (Br) causes similar effects. Br releases H from chopped human lung in vitro and contains a substance with similar physico-chemical behavior to methyl piperonylate (MP) (Hitchcock et al. Fed. Proc. 1971). We studied the capacity of compound 48/80 and MP to release H from human lung in vitro. In all experiments 0.5 or 1.0g chopped human autopsy lung obtained immediately post-mortem was incubated in tyrode at 37°, pH 7.4 for up to 1 hour. Average total H was 12.90 µg/g (n=19). Spontaneous release (SR) of H was linear for the first 20 min and continued to increase for up to 1 hour. Average SR was 1.67 $\mu g/g/30$ min (n=19). H released during incubation with 48/80 was concentration dependent. It was linear up to 2 mg 48/80 and reached a maximum at 3 mg. Average release with 2mg was 4.34 µg/g lung/30 min. Synthetic MP released H when incubated at FMC 5x10-11 to 5×10^{-5} . Optimum FMC was 5×10^{-8} when the average release of H was 1.32 $\mu g/g$ lung/30 min. Physiological amounts of H (1-5 µg) were not destroyed when incubated with chopped lung under the same conditions used for release. Addition of aminoguanidine at FMC 1x10-3 did not alter the amount of H released spontaneously or with 48/80. Thus, the release of endogenous pharmacologically active agents from human autopsy lung can provide clues about the pathogenesis of lung disease in man. Supported by USPHS Grant EC-00159.

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"BREATH BY BREATH" DETERMINATION OF CARDIAC OUTPUT. M.P. Hlastala, B. Wranne and C.J. Lenfant. Dept. of Med. and of Physiol. and Biophys., Univ. of Washington, Seattle, Wash., U.S.A.

Cardiac output is calculated from expired 0, and CO, concentrations and flow rate continuously monitored during a single non-extended expiration. This technique is a modification of that originally presented by Kim et al. (J. Appl. Physiol. 21(4):1338, 1966). We record the variables on analog magnetic tape for later interpretation using a digital computer. In this way, the accuracy has been improved to a sufficient degree to allow determination of cardiac output "breath by breath". During an expiration the alveolar PO, decreases at a relatively constant rate, while the rate of decrease of alveolar PCO, progressively drops. A linear relationship between PCO, and R (instantaneous gas exchange ratio) is established, which enables the estimation of mixed venous and arterial PCO. Using a modified Fick equation and the measured oxygen uptake for a single breath, the cardiac output is calculated. The cardiac output (mean ± SD), determined on separate occasions for ten to fifteen consecutive breaths, of three seated male subjects are: 5.98 ± .63 and 5.18 ± 1.01 L/min; 4.72 ± .90 and 4.62 ± 1.00 L/min; and 5.60 ± 1.67, 4.73 ± .90 and 5.70 ± .74 L/min. (Supported by USPHS Grants No. HE12174 and No. HE05819).

742 THE REACTIVITY OF MUSCLE PROPRIOCEPTORS TO STRECH AFTER CHRONIC DE-EFFEREN-TATION OR TENOTOMY.P.Hnik and M.-J.Lessler. Inst.of Physiology, Czechoslovak Ac.Sc., Prague and Dept.of Physiol.,Univ.of Utah, Salt Lake City, USA.

The slope of the integrated activity recorded from the muscle nerve per mm stretch is greater after chronic de-efferentation(D)(Hnik 1964), or tenotomy(T)(Eldred et al.1967), than in control muscles. An attempt has been made to analyse further the response to stretch of proprioceptive nerve endings in muscles undergoing atrophy after ventral root section, or tenotomy of the rat gastrocnemius muscle. While the frequency-extension curve from control muscles has a slope of 12.2/sec/mm, it was 21.2 in D and 32.1 in T muscles. During the period of stretching (5 mm at 10/mm/sec) the mean afferent frequency of discharge was also found to be increased in atrophying muscles. The value in control muscles was 29.4 imp./sec/mm, 42.3 in D and 63.3 in T muscles. This increased responsiveness to stretch of proprioceptors in D and T muscles is probably not due to compliance changes of muscle elements during atrophy, since the dynamic index in all three groups (control, D and T) was unchanged. (Supported by Grant NS 05666 from the U.S.Public Health Service). Ref. Hnik, P.: Physiol.bohemoslov. 13: 405, 1964; Eldred, E. et al.: In Neurophysiological Basis of Normal and Abnormal Motor Activities, Raven Press, New York 1967, p.35.

10NOGENIC GROUPS AT THE SURFACE OF THE HUMAN RED BLOOD CELL. D.G.Hoare, J.Riordan, G.F.Fuhrmann, and H.Passow, Max-Planck-Institut fuer Biophysik, Frankfurt (Main), Germany The electrophoretic behavior of the RBC surface is dominated by the carboxyl groups of neuraminic acid. In the pH range 3-10, the degree of dissociation of these groups and hence the electrophoretic mobility undergoes only a slight change. We investigated the effects of pH and chemical modification on neuraminidase-treated cells. After enzymatic treatment the charge in the plane of slip decreases with decreasing pH. At about pH 4.8, there is a charge reversal, indicating the presence of positive charges. Addition of formalin increases the negative net charge of the neuraminidase-treated cells at all pH values. The effects of formalin are partly reversible. The amino reactive agent trinitrobenzene sulfonate (TNBS) has similar effects, except that all the binding is irreversible. If added to TNBS-pretreated cells, formalin produces no additional effects. This suggests that at least part of the change in surface charge is due to interactions with amino groups. A study of the combined effects of formalin and SH-reagents shows that the results

The effect of the carboxyl groups in the RBC surface can also be overcome by their modification with carbodiinide and glycine ethyl ester. After abolishing the negative charge of neuraminic acid and protein carboxyl groups the sign of the surface charge is reversed over the whole pH range 3-10 and the absolute value of the electrophoretic mobility becomes similar to that of untreated cells. (Supported by the DFG, SFB 38)

cannot be simply explained by an abolition of fixed charges in a rigid surface. Chemical modification and pH changes seem to lift charged groups into or out of the plane of slip.

744 ENZYME MECHANISMS IN THERMAL ADAPTATION by P. W. Hochachka and T. Mustafa, Dept. of Zoology, Univ. of British Columbia, Vancouver, Canada.

Thermal compensation of metabolism in héterotherms can be achieved through i) immediate compensating mechanisms, ii) thermal acclimation, or iii) evolutionary adaptation. Immediate compensation of enzyme reaction rates depends on changes in apparent enzyme—substrate (E-S) affinities. The argument basically is one of kinetic versus thermo—dynamic control of enzyme reaction rates. In vivo substrate concentrations probably are lower than the K_m values for enzymes involved in their metabolism; regulation under these conditions is achieved by modulator-induced changes in E-S affinity. For many enzymes in heterotherms, low temperature acts in a manner analagous to the action of positive modulators, a decrease in thermal energy being compensated by appropriate increase in E-S affinity. Whereas E-S affinities tend to be thermolabile, enzyme-modulator interactions seem to be much more stable to temperature. Hence, control of catalysis also appears to be largely independent of temperature. At least in the case of Salmonid fishes, thermal acclimation appears to involve the production of new enzyme variants better adapted for controlled function in the new acclimation state.

EVIDENCE FOR THE PRESENCE OF STELLATE CELL INHIBITION IN FROG CEREBELLUM AND FOR MEDIATION OF THIS INHIBITION BY GAMMA AMINO BUTYRIC ACID.

B.J.Hoffer, G.R.Siggins, D.J.

Woodward and D.S.Rushmer. Lab. of Neuropharmacology, Natl. Inst. of Mental Health, St. Elizabeths Hosp., Washington, D.C. 20032 and Dept. of Physiology, Univ. of Rochester, Rochester, N. Y. U.S.A.

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In most vertebrates, local electrical stimulation of the surface of the cerebellum (LOC) is thought to inhibit Purkinje (P) cell discharge by parallel fiber excitation of the interneurons of the molecular layer. In frogs which are curarized, locally, anesthetized and artificially respired, LOC stimulation produces an inhibition in P cell discharge often lasting several hundred milliseconds and accompanied by a hyperpolarization of the P cell membranes, analogous to such inhibition in other species. Microiontophoresis of gamma amino butyric acid (GABA) from multi-barreled micropipettes mimics the effects of interneuron inhibition, producing cessation of P cell discharge accompanied by hyperpolarization and decreased membrane resistance. Microiontophoresis of picrotoxin or bicuculline, but not strycnnine, antagonized P cell responses to GABA, and reproducibly blocked the inhibitory effects of LOC stimulation on P cell spontaneous discharge. These experiments suggest that LOC induced inhibition does exist in froq cerebellum, and that GABA may be the inhibitory neurotransmitter released by molecular layer interneurons.

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PLASMA MEMBRANE POTENTIALS IN AMPHIUMA RED CELLS. Joseph F. Hoffman and Ulrik V. Lassen. Zoophysiological Lab. B, University of Copenhagen, Copenhagen, Denmark.

Membrane potentials across the giant red cells of Amphiuma were measured with microelectrodes driven intracellularly with a piezoelectric device (J. Physiol. 195: 681, 1968) modified to increase the response time so that rapid changes in membrane potential could be resolved. Upon impalement the potential characteristically peaked within 200 usec and fell transiently in 1 to 2 msec to remain stable for at least 50 msec. The stable level potentials were small and negative (relative to outside) and varied little with change in conditions. In contrast, peak potentials changed in accordance with predictions based on the measured Donnan distribution of chloride, becoming more negative (relative to outside) as the pH of the medium (Ringers) was varied from 6.5 to 7.9. quantitative agreement takes into account the fact that the chloride is in higher concentration in the cytoplasm than in the nucleus. The peak potential also changed sign systematically, going markedly positive, as the medium chloride was lowered by substitution with the impermeant anion, p-aminohippurate. The peak potential was not affected by metabolic or transport inhibitors. Surprisingly, valinomycin (10-6M) changed the membrane characteristics from that of a Cl electrode to that of a K electrode. The fall in peak potential presumably reflects electrical leakage around the microelectrode while the stable level reflects a complex diffusion/junction potential. Estimates of the membrane resistance of these cells will be discussed in relation to their chloride permeability.

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HEPATIC METABOLISM OF DEHYDROCHOLIC ACID IN MAN. A.F.Hofmann, R.D.Soloway, P.J.Thomas, and L.J.Schoenfield. Gastroenterology Unit, Mayo Clinic and Mayo Fndn., Rochester, Minn., and P.D.Klein. Division of Biol. and Med. Res., Argonne Natl. Lab., Argonne, Ill., U.S.A.

For many years, dehydrocholic acid (3,7,12-triketo-5β-cholanoic acid--triKC) has been used to stimulate bile flow in man. Since triKC does not form micelles, choleresis has been assumed to result from an increase in osmotic flow. The suggestion of Hardison that triKC is metabolized during passage through the rat liver stimulated us to define its metabolism by the liver in man. To do this, we synthesized and administered intravenously 24-14C-triKC to a patient with a bile fistula; 80% of administered radioactivity was recovered in bile, entirely as glycine and taurine conjugates of bile acids different from triKC. After enzymatic or alkaline hydrolysis, radioactivity was present in three metab-68% as 3α,7α-dihydroxy-12-keto-5β-cholanoic acid (I); 26% as 3α-hydroxy-7,12olites: diketo-5β-cholanoic acid (II), and 5% as cholic acid. Structure was deduced by thin-layer and gas chromatography, and proved by combined gas chromatography/mass spectroscopy. Confirmation of structure was obtained by co-chromatography of methyl esters of I and II with synthetically prepared 3 H-methyl esters, as well as by crystallization of I and II to constant 3 H/ 1 C ratios. Thus, in man, triKC was rapidly reduced stereospecifically to α-hydroxy-keto and cholic acids during passage through the liver. Relative reduction rates were: 3 keto:7 keto:12 keto::20:15:1. We conclude that choleresis caused by triKC administration cannot be explained by the physical properties of triKC, and we speculate that one of the metabolites identified may induce bile secretion.

748 COMPARISON OF HEAT-INDUCED HYPERVENTILATION IN THE SHORN AND UNSHORN SHEEP. W. F. Hofman and G. D. Riegle. Endocrine Res. Unit, Michigan State Univ., E. Lansing, Mi. and Dept. of Physiology, Med. Col. of Georgia, Augusta, Ga., U.S.A.

During heat stress, sheep increase respiratory activity (panting) in order to facilitate evaporative heat loss from the upper respiratory tract. Although an increase in alveolar ventilation (\hat{V}_A) has been found to accompany thermal polypnea (Hales and Webster, J. Physiol. 190: 241) a simultaneous quantitative assessment of respiratory evaporative heat loss has not been reported. In the present study, three, 3 year old, non-gravid, unanesthetized Dorset ewes with surgically exteriorized carotid loops were exposed shorn (less than 0.3cm of fleece) and unshorn (7.0cm of fleece) to ambient temperatures (T_a) of 25, 30, 35 and 40°C with a constant 40% relative humidity. Thermal and respiratory responses to each level of heat stress were indexed during the last 30 minutes of a 120 minute whole body exposure by measurements of rectal (T_{re}) and 6 skin temperatures (T_{re}), respiratory frequency (f), oxygen consumption (T_{re} 0), respiratory evaporative heat loss (E), heart rate and mean arterial blood pressure; arterial blood samples were analyzed for H⁺ and Paco2. Both shorn and unshorn animals exhibited progressive increases in T_{re} 's and T_{re} 's as T_{re} increased. Even though f increased for shorn and unshorn sheep as T_{re} 0 was elevated, tidal volume (T_{re} 1) decreased in the shorn animal and increased in the unshorn sheep. Only in the unshorn animal were elevations in E accompanied by increases in T_{re} 0, attendant to an increased T_{re} 1 and resulting in a progressive respiratory alkalosis as T_{re} 2 was raised.

749 EFFECT OF CALCIUM ON AUTOMATICITY IN CANINE PURKINJE FIBERS. P. M. Hogan and S. L. Sinclair. Dept. Physiology, State Univ. of New York at Buffalo, N. Y., USA.

Increases in extracellular calcium concentration are known to increase the spontaneous rate of isolated hearts, suggesting a direct membrane effect of calcium on cardiac pacemaker cells. To test this possibility transmembrane potentials of isolated, perfused canine Purkinje fibers were continuously monitored for changes in the electrophysiological parameters of automaticity as a function of extracellular calcium concentration. Preparations were driven electrically at a rate of 90/min as the extracellular Ca++ concentration was raised from 2.7 mM to 16.2 mM in Tyrode solution. Increased Ca++ caused a decrease in maximum diastolic potential (shift toward zero potential) and a simultaneous increase in the rate of slow diastolic depolarization. These changes favor an increased firing rate in spontaneously beating fibers. Furthermore, threshold potential decreased with increased extracellular Ca++, thereby limiting the overall increase in automaticity. Similar changes in the parameters of automaticity could be observed during short periods of rapid drive at a given level of elevated extracellular Ca++. During periods of rapid drive the Ca++ induced changes were increased, but reverted quickly upon return to the basic drive rate. The degree of such transient enhancement was directly proportional to the rate of rapid drive. The changes in maximum diastolic potential and slow diastolic depolarization were opposite to those observed during rapid drive in control Tyrode solution. It appears that increases in extracellular Ca++ may cause rate-dependent enhancement of automaticity in the canine Purkinje fiber.

750 POTASSIUM EXCHANGE ACROSS THE GASTRIC MUCOSA. C. Adrian M. Hogben, Dept. of Physiology and Biophysics, University of Iowa, Iowa City, Iowa 52240

A high extracellular (ECF) K, 70 mEq/l, at the serosal surface of the bullfrog gastric mucosa reverses the electrical transmucosal PD. This has erroneously been attributed to the serosal face of the epithelium being selectively permeable to K (§ Cl). It has been shown that the high ECF K inhibits active transport of Cl. It is not a simple osmotic effect. Present studies reveal that about one half of the effect of K on the PD is due to downhill movement of K, l $\mu \text{Eq/sq.cm/hr.}$ A high ECF Rb similarly reverses the PD and the short-circuit current. A small part of the change is due to the removal of Na to accomodate additional K. With normal and the same concentrations of K on either side of the mucosa, 2.5 or 5 mEq/l, there is a net absorption of K through the short-circuited mucosa with net fluxes of 0.09 § 0.14 $\mu \text{Eq/sq.cm/hr.}$ and flux ratios of 4 § 5 respectively for the two concentrations. The apparent fluxes appear to reach a steady state before tissue cell K has equilibrated. (Supported by NIH Grant AM 05848)

POTASSIUM-ESCAPE-PHENOMENON DURING CONTINUOUS TREATMENT WITH AMILORIDE IN RATS. $\underline{\text{M. Hoheneqqer}}$. Institute of gen. and exper. Pathology, University of Vienna, Austria.

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The potassium-escape-phenomenon during continuous treatment with amiloride revealed some striking similarities with the sodium-escape-phenomenon as seen during mineralocorticoid administration which was first observed in Kramer's school. In rats, pretreated with a low potassium diet (0.07%), the period of potassium retention during continuous amiloride treatment was dependent upon the daily potassium intake. With a daily potassium intake of 73 µeq per 100 g body weight, retention of potassium was observed for 4 - 5 days, whereas with an intake of 1200 µeq per 100 g body weight the potassium retaining period was only 2 days. In rats pretreated with a diet of normal (0.5%) or enriched (1.0%) potassium content, the period of potassium retention during amiloride treatment was further shortened. The potassium-escape phenomenon was not modified by adrenal-ectomizing the rats. Acid-loading and even more alkali-loading led to a remarkable shortening of the potassium-retention-period. In normal rats, serum potassium levels during amiloride administration remained always in the normal range, except in those animals which were loaded with ammonium-chloride.

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DISTRIBUTION OF GLUTAMATE DEHYDROGENASE (GLUDH) AS AN INDEX OF MITOCHON-DRIAL ENERGY PRODUCTION IN THE NEPHRON OF THE RABBIT. B Höhmann, V. Schreiber, H. Bindewald Kinderklinik Univ Freiburg, Germany.

Using the isolation technique of BURG and ORLOFF twelve different seg-

ments of the nephron could be isolated, in which enzyme activities were measured by methods of quantitative histochemistry according to LOWRY. In addition to dry weight as a reference point (values in brackets) enzyme activities could be related to the length of the segments. This allows direct comparison with transport data also given per tubular length. The highest activity of GluDH which links amino acid metabolism to the citric acid cycle was found in the proximal convolution. In other segments the activity relative to proximal convolution (100%) was: beginning of thin loop of Henle 9 (20)%, thick ascending limb 10 (30)%, distal convolution 15 (75)%, cortical collecting duct 30 (80)%, collecting duct medulla 5 (24)%, collecting duct papilla 2 (16)%. High activity in the cortical part of the nephron and the difference between the distribution of Na*-K*-ATPase and GluDH leads to the suggestion that GluDH does not have a constant proportion to mitochondrial citric acid cycle enzymes throughout the tubule but is relatively concentrated in those segments in which ammonia is formed.

EFFECT OF SEX HORMONES AND PROLACTIN ON SEX BEHAVIOUR AND GROOMING IN FE-MALE RHESUS MONKEYS. E.Otto Höhn. Dept. of Physiology, University of Alberta, Edmonton, Canada.

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After ovariectomy, mounting and presentations virtually ceased after 10-108 days after the operation in six animals. In another, mounting recurred, and in another, it had not disappeared at 105 days after ovariectomy; adrenal inhibition with dexamethasone did not abolish sex behaviour in either of these animals. Estradiol (5 μ g daily) restored mountings and presentations in six animals but failed to do so, even in 15 μ g doses, in another. Treatment with estradiol and progesterone reduced mountings, presentations and male mounting attempts refused by the females and increased grooming in both sexes. The changes in sex behaviour were not due, as in the observations of others, to increased female refusals but reduced male initiative. Estradiol and prolactin (20 μ g) reduced mountings, presentations and refused mountings, but had little effect on grooming. Testosterone (1mg daily) reduced frequency of mountings, presentations and refused mountings; 5 mg daily in one animal also failed to stimulate presentations as reported by others; effects on grooming were insignificant. Only two out of five males and three out of seven females groomed or were groomed by their partners.

754 SPECTRAL ANALYSIS OF NEURONAL INTERACTIONS. A.V.Holden and A.S.French. Dept. of Physiology, Univ. of Alberta, Edmonton 7, Canada.

A necessary preliminary to understanding the neuronal basis of elemental acts of behaviour is a quantitative description of the dynamics of interactions between single neurones. Neuronal spike trains can be considered as stochastic point processes, and digital spectral analysis may be used to characterize such random signals and to quantify the relations between them. For two such signals x(t) and y(t) the auto-spectra Sxx(f), Syy(f) and the cross-spectra Sxy(f), Syx(f) may be estimated. If the two signals are causally related we can estimate from these spectra the frequency response function g(f) = Sxy(f)/Sxx(f) or Syy(f)/Syx(f), and the coherence function g(f) = Sxy(f)/Sxx(f). Syy(f). These measures quantitatively describe the dynamic relationship between the two signals. Techniques for consistent, alias-free and bias-free spectral estimation of neuronal spike trains have been developed and these techniques have been applied to neural analogs, insect mechanoreceptors and an insect proprioceptive reflex. Supported by the M.R.C. and Muscular Dystrophy Association of Canada.

DEVELOPMENTAL AND BEHAVIORAL EFFECTS OF BRAIN 5-HYDROXYTRYPTAMINE DEPLETION IN RAT PUPS. K. Hole. Inst. of Physiology, Univ. of Bergen, Bergen, Norway. Rats depleted of brain 5-hydroxytryptamine (5-HT) to 20% of control values by injections of p-chlorophenylalanine (pCPA) in the first 7 weeks of life showed a decrease in brain weight, and also behavioral deficits when tested 4-7 weeks after injections. All behavioral deficits in the tests (spontaneous alternation, activity test, open field, habituation to auditory stimulation, Lashley III maze, and passive avoidance) could be explained by postulating a decrease in arousal level in the pCPA treated rats. In a second experiment rat pups were injected either with pCPA or with L-phenylalanine (PA) from 6-14 days of age. Both procedures decreased brain 5-HT (pCPA:to 27%, PA:to 63% of control values), and the brain weight was also significantly decreased (pCPA:to 79 %, PA:to 85% of brain weight of controls) Additional injections of 5-hydroxytryptophan during the same age period (6-14 days), partly restoring brain 5-HT contents, also had a protective effect against the decrease in brain weight produced by pCPA or PA, confirming the importance of 5-HT depletion for the decreased brain growth in both preparations. The low brain 5-HT in phenylketonuria may be at least one of the important factors yielding the brain damage in this disease. Drugs depleting brain 5-HT should not be used in children in the first 2-3 years of life, or during pregnancy.

756 TEMPERATURE EFFECT ON RATE OF UPTAKE OF CARBON DIOXIDE BY HUMAN RED CELL SUSPENSIONS.
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University of Pennsylvania, Philadelphia, Pa., U.S.A.

The rate of uptake of $\rm CO_2$ by human red cells was measured using a continuous-flow rapid reaction apparatus. A suspension of red cells ($\rm HbO_2 \approx 1.8C_3$) was adjusted to a pH value of 7.8 ± 0.2 in saline. Its initial $\rm CO_2$ tension was zero. This suspension was rapidly mixed with a buffer containing 30 mM $\rm HCO_3^-$ at a $\rm CO_2$ tension of approximately 90 mm Hg. The time course of the fall of $\rm PCO_2$ in the mixture of reactants was followed with a $\rm CO_2$ electrode placed at different distances downstream. The hemoglobin was fully oxygenated throughout and when the reaction was complete the fall in $\rm CO_2$ tension was about 16 mm Hg. At all temperatures, the first half of this reaction proceeded rapidly. At 42°C the initial rate corresponded to a half-time of 12 msec; at 26°O and 12°O the corresponding half-times were 21 and 34 msec. Acetazolamide slowed the entire reaction thus excluding carbamate formation as a cause of the initial rapid fall of PCO_2. At low temperature the second half of the reaction was much slowed so that the reaction was only two-thirds complete after one second. The results suggest that, at low temperatures, slowness of the chloride shift may prevent $\rm CO_2$ equilibrium being attained during blood passage through capillaries.

OXYGEN UPTAKE DURING SWIMMING AT DIFFERENT SPEEDS. I. Holmér and P.-O. Astrand. Dept. Physiology, Gymnastik- och idrottshögskolan, Stockholm, Sweden.

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In a newly constructed basin water can be circulated in a 2.5 m wide and 1.2 m deep vertical loop by two horizontal variable pitch axial flow pumps located in the part of the loop below a test basin, which is 4.0 m long. This swim-mill provides unic and excellent possibilities to study the physiology and biomechanics of swimming since the speed can be varied and reproduced with great accuracy, and still the subject swims on the same spot. Oxygen uptake, pulmonary ventilation, and heart rate were measured for 6 subjects when swimming with various styles. Furthermore similar measurements were done during submaximal and maximal work on treadmill and bicycle ergometer. The underwater weight of the subjects was determined by hydrostatic weighing. The highest V_{02} was attained during running (100%), followed by bicycling (95%), and the maximum lowest was whilst swimming (87%). For the two swimmers of European top class, the values for V_{02} were for the male 5.59 liters/min (100%) during running 5.11 liters/min (91%) during bicycling and 5.08 liters/min (100%) respectively. The study confirmed previous findings of free style as the most economical style.

CHARACTERISTICS AND ION TRANSPORT FUNCTIONS OF CARBONIC ANHYDRASE ACTIVITY IN RAT LIVER MITOCHONDRIA, F.A. Holton. Dept. of Physiology, Royal Veterinary College, University of London, Royal College Street, London, NW1 OTU, England.

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Isolated rat liver mitochondria catalyze the hydration of carbon dioxide. The catalyst responsible is unlike the carbonic anhydrase of erythrocytes in being membrane bound and also in being less sensitive to inhibitors. Diamox (acetazoleamide) does not inhibit the mitochondrial catalyst while sulphanilamide and para-toluenesulphonamide are relatively weak inhibitors. The study of mitochondrial respiration in acid-pulse experiments has shown that mitochondrial carbonic anhydrase activity can facilitate choline movement across the inner membrane of the mitochondrion, probably by accelerating the alternate dehydration of external bicarbonate ion and the hydration of internal carbon dioxide. These results suggest that the normal function of the mitochondrial catalyst may be to participate in ion transport across the mitochondrial membrane.

SUBSTANCES LIBERATED BY THE NERVOUS SYSTEM OF PERIPLANETA AMERICANA - L: E:L. Holzacker and O.Giannotti - Instituto Biológico - Brasil

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The isolated subesophageal, pro-, me so-and metathoracic ganglions suspended in physiological solution release substances absorbing at 210, 235 and 285 m/s. The quantity liberated per ganglion is extremely variable. These substances were not found / when the other tissues such as the muscles of neck, femur and trochanter or the adipose tissues of the thorax were treated under the same conditions. These substances can be dialyzed, are soluble in water and methanol, insoluble in less polar solvent. It seems to be stable at 100° C (as judged by the U.V. spectrum). Preliminary relationships between the amount liberated and nerve excitation will be presented.

DOES PREGNENOLONE PLAY A SIGNIFICANT ROLE IN THE REGULATION OF STER-OIDOGENESIS BY ACTH? M. Holzbauer and J. Urquhart. ARC Inst. of Animal Physiology, Babraham, England, and Univ. of Southern California, Los Angeles, Calif., USA.

Pregnenolone can be demonstrated in vitro to inhibit cholesterol hydroxylation. Because the rate-limiting step for adrenal steroidogenesis appears to be cholesterol hydroxylation, its inhibition by the steroidogenic intermediate, pregnenolone, might be of major significance in mediating the regulation of steroidogenesis by ACTH in the intact adrenocortical cell. If that were true, high rates of steroidogenesis ought to be associated with low adrenal contents of pregnenolone, and vice versa. We sought to test that idea by making simultaneous measurements of cortisol and pregnenolone secretion rates, and, immediately thereafter, of adrenal gland pregnenolone content. Several experimental designs were used: measurements were made on single perfused canine adrenals at first low and then high rates of steroidogenesis (and vice versa); also measurements were made on each adrenal gland of dogs before, and at various times after, hypophysectomy. The results show that adrenal pregnenolone content and secretion rate rise in approximate proportion to cortisol secretion rate. We considered the possibility that mitochondrial pregnenolone content might change in a direction opposite to total gland content, but the data, together with reasonable assumptions, do not support that view. CONCLUSION: Whatever the inhibitory action of pregnenolone on cholesterol hydroxylation in vitro, this action does not appear to play a significant role in intact adrenocortical cells. (Supported by ARC, NIGMS and General Technical Services, Inc.)

761 EVALUATION OF PERITUBULAR CAPILLARY MICROPERFUSION (PCM) METHOD. H. Holzgreve, R.W.Schrier and L.E. Earley. Dept. of Medicine and CVRI, Univ. of California, San Francisco, Calif.

Conflicting results obtained with some micropuncture techniques could be due to undefined technical errors. In the present study the following possible sources of error in the newly developed method of PCM were examined: 1) obstruction of efferent capillary blood flow and consequent cessation of glomerular filtration by aggregation of red blood cells, 2) "back-filtration" of peritubular perfusate and contamination of tubular fluid, and 3) incomplete artificial PCM of proximal convolutions under study. Methods included injection of colored latex into surface efferent arterioles, the renal artery and renal tubules with subsequent microdissection. Peritubular capillaries were perfused with lissamine green over a range of 150 to 20,000 nl/min in search of "back-filtration". The results demonstrated: 1) obstruction of efferent capillary blood flow is not a source of error because a) only 25% of efferent capillaries and tubules which are punctured belong to the same glomerulus, b) efferent capillaries frequently give branches prior to the site of puncture on the kidney surface, c) blood flow continues out of the efferent capillaries around the perfusion pipette, 2) "back-filtration" and contamination of tubular fluid does not occur at perfusion rates up to 20,000 nl/min but was observed occasionally during rapid manual injection of lissamine green under high pressure, 3) incomplete PCM of proximal convolutions under study is a potential hazard and must be excluded in each instance.

762 EFFECTS OF CAFFEINE ON EXCITATION-CONTRACTION-COUPLING IN MAMMALIAN AND IN FROG'S MYOCARDIUM. H.Homburger and H.Antoni (Inst. of Physiology, University of Frankfurt/M. German Fed. Rep.).

Mammalian myocardium exhibits characteristic mechanical reactions (delayed response to modifications of action potential duration, postextrasystolic and poststimulation potentiation etc.) which may be attributed to calcium-dependent processes in the sarcoplasmic reticulum (SR). In the frog's myocardium where SR is poorly developed or absent, no comparable responses are demonstrable (1). Caffeine (10 mM/1) specifically abolishes these characteristic responses of the mammalian myocardium (papillary muscle of guinea pig) whereas the frog's heart is little affected. Under smaller doses of caffeine (1-5 mM/1) the mammalian myocardium shows a persistent positive inotropic response associated with prolongation of the electromechanical latency and reduction of the early rate of rise of isometric tension. These findings suggest that caffeine may interfere with the fast coupling system represented by the SR. They are consistent with the observation of reduced uptake and/or augmented release of Ca by SR fractions (2).

References: (1)H.ANTONI, R.JACOB and R.KAUFMANN: Pflügers Arch. 306,33(1969) (2)A.WEBER and R.HERZ: J.Gen. Physiol. 52,750(1968).

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STRETCH REFLEX DURING MUSCLE VIBRATION.
S. Homma and K. Kanda. Dept. of Physiol., School of Med., Chiba Univ., Chiba, Japan.

Chiba, Japan.

It has been demonstrated in cat that primary spindle endings are very sensitive to muscle vibration and group Ia afferent discharges elicited by vibration activate spinal motoneuron monosynaptically. It has been also reported that vibration of muscle tendon on the human subject causes gradual increase of muscle tension, that is called as tonic vibration

reflex (Hagbarth & Eklund, 1965).

In cat, the reflex discharge was recorded from a single ventral root fiber during muscle vibration. Nonsequential histogram showed that spike intervals distributed around integer multiplication of vibratory cyclic time. Therefore, the muscle tension of T.V.R. is produced by the muscle spike discharge having such inter-spike intervals. A gradual increase of muscle tension during vibration is explained by the shortening muscle spike intervals at integer multiplication of vibration frequency.

POSTOCCLUSIVE REACTIVE HYPEREMIA IN THE ISOLATED PERFUSED KIDNEY OF RABBITS. <u>Mishio Honda</u>. 1st Dept. of Med., Univ. of Tokyo Sch. of Med., Tokyo, Japan.

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Postocclusive hyperemia was studied in the isolated rabbit kidney perfused with Characteristically, two phases of vascular response were revealed oxygenated blood. after release of the arterial occlusion: an initial phase of transient vasodilation and succeeding vasoconstriction, and a second phase of gradually developed vasodilation. The duration of the initial phase averaged 15 sec following 1-min occlusion. The initial vasoconstriction was ordinarily demonstrated in the renal autoregulatory range above 100 mm Hg. Moderately increased vascular tone, made by infusions of noradrenaline and angiotensin II, favored the production of the initial vasoconstriction, whereas depressed vascular tone, made by the infusion of papaverine, abolished it. With longer occlusion periods, the imitial vascular response was reduced. The second hyperemic response was slower in development and more persistent than the initial phase. magnitude of the second phase rose with progressively longer occlusions. Reperfusion with anoxic blood, on release of the occlusion, did not significantly affect recovery from the hyperemia. The intraarterial injection of metabolic inhibitors modified the second hyperemic response. The findings suggest that both myogenic and metabolic factors are responsible for the production of reactive hyperemia in the rabbit kidney.

ALVEOLAR GAS EXCHANGES AND CARDIOVASCULAR FUNCTIONS DURING BREATH-HOLDING WITH AIR. S.K. Hong, Y.C. Lin, D.A. Lally and T.O. Moore. Dept. of Physiology, Univ. of Hawaii Sch. of Med., Honolulu, Hawaii, U.S.A.

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During 4 min breath-holding (BH) with TLC or 160 sec BH with FRC PAO2 decreased continuously, reaching approximately 30 mm Hg at the end, while PACO2 increased during first 30 sec after which it leveled off at approximately 50 mm Hg. During 4 min BH the lung supplied 700 ml of 02 into the blood while it gained only 160 ml of CO2 from the blood, indicating a significant retention of CO2. Both PaO2 and PaCO2 changed during BH in a manner similar to those of alveolar gas. (A - a)O2 gradient was approximately 10 mm Hg throughout the entire BH period, while the usual (a - A)CO2 gradient was reversed during BH. Arterial O2 content decreased by 12.5 vols % and CO2 content increased by 17.0 vols. % during 4 min BH. Mixed venous O2 pressure and content approached arterial blood values toward the end of BH. On the other hand, mixed venous CO2 pressure and content approached arterial values after 30 to 60 sec of BH. The pulse pressure tended to increase toward the end of BH. The heart rate decreased by 15% within 20 sec and was maintained at this level until the end of BH. Cardiac outputs measured during 1.5 to 2 min BH by dyedilution method were not significantly different from those measured before BH. (This investigation was supported in part by NSF Sea Grant No. GH-62.)

766 FAST TRANSMISSION OF LABYRINTHINE INPUT TO OCULAR MOTONEURONES. G.Horcholle-Bossavit and S.Tyĉ-Dumont. Physiol.Dept., Fac.Med.St-Antoine, Paris, France.

Electrical characteristics of the transmission of labyrinthine volleys to abducens motoneurones are studied in the unanesthetized "encéphale isolé" cat using extracellular and intracellular microelectrodes. Single shock stimulation of the ampulla of the left semicircular horizontal canal evokes field potentials from the VIIIth nerve recorded centrally just after its entry into the pons and from the contralateral MLF fibers. Both responses appear with latencies of 0,3ms and 0,6ms respectively. The rapidity of the MLF response is confirmed by recording intraxonic action potentials from MLF fibers at a latency of 0,56ms. The admitted disynaptic vestibulo-ocular reflex arc with a synaptic delay of 0,4ms in the medial vestibular nucleus does not fit with the early MLF field potential described here Neither a monosynaptic link between labyrinthine receptors and ocular motoneurones nor the antidromic excitation of efferent fibers passing through the abducens nucleus seem satisfactory hypothesis to explain a fast transmission since no response can be triggered from the VIIIth nerve while stimulating the MLF. We suggest that an electrotonic coupling might exist in the nystagmic network that determines periodic eye movements. Arguments for speculating about an electrotonic coupling can be found in the phylogenetical history of vestibulo-ocular systems and also in a growing body of anatomical data showing the occurrence of gap junctions in the nervous system of mammals. The function of gap junctions would be to provide a quick-acting mechanism for synchronization in a rhythmic system.

767 ACTIVATION AND INHIBITION OF VASOCONSTRICTORS IN SKIN AND MUSCLE NERVES UPON STIMULATION OF SKIN RECEPTORS. Horeyseck, G., Jänig, W., II. Physiologisches Inst., Heidelberg, Germany.

Postganglionic sympathetic fibres in nerves from the hairy skin and the muscles of the hindlimb of the cat were dissected and identified by stimulation of the lumbar sympathetic trunk. The spontaneous activity in these fibres was inhibited by stimulation of the ipsilateral depressor nerve; thus, these fibres were most probably vasoconstrictors. Natural stimulation of skin receptors of hindlimbs which excited Gr. II, III and IV afferents produced response patterns of opposite nature in sympathetic fibres in skin and muscle as follows: (1) Postganglionic fibres in skin nerves were excited by stimulation of hairfollicle receptors and inhibited by stimulation of mechano-nociceptors and heat receptors. (2) Postganglionic fibres in muscle nerves were inhibited by stimulation of hairfollicle receptors. Stimulation of cold and warm receptors and Pacinian corpuscles located subcutaneously did not change the spontaneous activity in both types of fibres. Stimulation of slowly adapting mechanoreceptors in the pad had no definite excitatory or inhibitory effect on the activity of these fibres. (Supported by the Deutsche Forschungsgemeinschaft).

768 ELECTRICAL RECORDING FROM DENTINE. H.Horiuchi and B.Matthews. Dept. of Physiology (Oral Biology), Univ. of Bristol, ENGLAND BS8 ITD.

It has been claimed that receptor potentials and nerve impulses can be recorded with an electrode in contact with the floor of a cavity in dentine (Scott,D. & Tempel,T., J.Dent.Res.44,20-27,1965; Matthews,B., Archs.oral Biol.15,523-530.1970). However, it is known that voltage changes with similar waveforms may be generated as noise at certain electrode/electrolyte interfaces (Flasterstein,A., Med.& Biol.Engng.4,583-588, 1966) and we have shown that the techniques used to record from dentine are subject to this type of noise, indicating that some of the activity previously assumed to be of neural origin might be artefact. It is nevertheless clear that individual nerve action potentials can be recorded from dentine. This has been established in cats by isolating from the inferior dental nerve a single fibre that responded to electrical stimulation of the dentine then applying the electrical stimulus to the nerve filament and showing that a single unit response with the same latency could be recorded from dentine. Using a similar preparation it has been possible, by collision, to block the response to electrical stimulation of the nerve when the stimulator was triggered by a 'spontaneous' impulse recorded from dentine.

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THE ROLE OF Ca⁺⁺ IN EXCITATION OF VASCULAR AND OTHER SMOOTH MUSCLE. L. Horn, M. Kumamoto and A. Nakajima. College of Medicine and Dentistry of New Jersey at Newark, Newark, New Jersey 07103 and Kyoto University, Kyoto, Japan.

Electrical properties of the longitudinal muscle fibers from the superior mesenteric vein and the taenia coli of the guinea pig has been investigated using intracellular recording, voltage clamp, and constant current injection techniques. Normal spontaneous electrical activities and responses to catecholamines and acetylcholine (Ach) are compared. The reversal potential of Ach in vascular muscle was found to be substantially more negative than that for skeletal muscle and nerve, and somewhat lower than that of taenia coli. The effects of Tetrodotoxin (TTX), Mn++ and graded changes in Ca++-concentration on the two preparations are discussed. It is suggested that the excitation in both preparations is obligate Ca++-dependent, inhibited by transition metals that interfere with Ca++-permeability and that it is unaffected by TTX. (This work has been supported by a general research grant from NSF, a grant from The New Jersey Heart Association and support from U.S.-Japan Cooperative Scientific Program, Office of International Activities, N.S.F.).

THE EFFECT OF CERVICAL SPINAL CORD TRANSECTION ON THE DC-POTENTIAL DIFFERENCE BETWEEN LUMBAR CEREBROSPINAL FLUID AND BLOOD IN DOGS. T.F. Hornbein and S.C. Sørensen. Institute of Medical Physiology, University of Copenhagen, Copenhagen, Denmark.

In the dog the DC-potential (E) between cerebrospinal fluid and blood (CSF-blood) increases linearly with decreasing blood pH. For ventilatory-induced changes in arterial pH the magnitude of this response ($\Delta E/\Delta pHa$) is -40.6, -26.7 and 5.0 mV/pH when measured respectively from lateral venticle, cisterna magna, and lumbar sac to jugular venous blood (Hornbein and Sørensen, Fed. Proc., 1971). To determine whether the low $\Delta E/\Delta pHa$ in the lumbar sac is created in the spinal cord or simply reflects changes in E in the brain, we measured lumbar $\Delta E/\Delta pHa$ before and after ligation and transection of the spinal cord and dura in the cervical region. In all studies $\Delta E/\Delta pHa$ was preserved following cervical cord transection, the mean value $\pm se$ (n=4) being 4.1 \pm 0.9 before, and 3.6 \pm 0.2 mV/pH after sectioning. This finding suggests that the pH sensitive E is a property of the "blood-brain barrier" independent of a possible pH-sensitive E across choroid plexus.

(Supported by Univ. of Copenhagen and USPHS, NHLI RCDA 5-K3-HE-9617 and NIGMS 15991-03).

LIGHT SCATTERING CHANGES ASSOCIATED WITH ACTIVATION OF SINGLE FROG SKELETAL MUSCLE FIBERS. P. Horowicz, F. Bezanilla, C. M. Armstrong, Dept. Physiol. Univ. Rochester, Rochester, New York U.S.A.

Light scattered along the fiber axis from an illuminated cross section was measured, using an optical system similar to that described by Blinks. A slit was focused onto the fiber, illuminating the cross section for 20 to 50 microns along the axis. Light was gathered (at 90° to the incident beam) by a lens of wide aperture and long working distance. Cross section image could be examined, or it could fall on a photomultiplier whose output was fed to an averager. Tension was measured with an RCA 5734 tube. Stimulation was usually by transverse current. To eliminate vertical and horizontal movement, the fiber was stretched over a pedestal. Axial movement could not be prevented. Averaging 100 to 250 twitches at .5/sec. we find a consistent scattering decrease usually beginning before there is discernible tension. This is followed by a variable increase, which may be in part the result of movement. Hyperpolarization of a resting fiber by 70 mV for 20 ms caused no measurable scattering change (approximately 2000 pulses). Depolarization of a fiber with low resting potential by 100 mV caused no contraction and no measurable scattering change. We conclude that the early scattering decrease is associated with fiber activation, and not with the action potential. Supported by USPHS NS 08893-01.

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772 MICROPUNCTURE STUDIES ON THE POSTNATAL DEVELOPMENT OF NEPHRON FUNCTION. Michael Horster. Physiologisches Institut der Universitat Munchen, Germany, and Dept. Physiology, Dartmouth Medical School, Hanover, N.H. USA

Postnatal maturation of glomerular and tubular function was studied in 26 dogs of a pure-bred beagle strain, 2 to 77 days of age. Renal function and systemic arterial pressure were monitored continuously. Whole kidney GFR increased linearly with age, from 0.13 ml/min per g kidney at two days to 0.91 at 77 days. EpAH increased from about 20 to 80%, and RPF (CpAH/EpAH) per g kidney increased threefold during the same period, resulting in a rise of FF during the early postnatal period. Superficial tubules, representing the youngest nephron generation, were found to be uniformly perfused at the end of the third week after birth. GFR of single superficial nephrons (n=103) increased sevenfold from 3.2 nl/min at 21 days to 23.1 at 77 days, while TF/P_{In} at 40 to 50% proximal tubular length was constant at mature value. Stop-flow pressure in single nephrons was constant with age (37.5 + 4.9 mmHg), as was intratubular pressure, while peritubular hydrostatic pressure increased from 3.7 mmHg at 13 days to 9.2 at 40 days. Proximal tubular diameter and length increased by factor 3 and 2, respectively. Conclusions: a) the postnatal increase in glomerular filtration rate at arterial pressures between 90 and 130 mmHg is primarily due to changes in the glomerular capillary membrane, b) the fraction of filtrate reabsorbed in the proximal tubule in antidiuresis is constant at mature level from the onset of postnatal tubular perfusion, in face of changes in filtered load, in peritubular hydrostatic and plasma-oncotic pressures, and in proximal tubular volume. (Supported by the National Kidney Foundation, New York)

773 CHARACTERISTICS OF UNIT RESPONSES OF THALAMIC NUCLEI DURING ELICITED SPINDLES.
F. E. Horvath and P. Buser. Lab. of Comp. Neurophysiology, Univ. of Paris, Paris, France.

Unit recordings were taken from neurons in various thalamic nuclei. Of the 360 neurons investigated, 280 or 78% were responsive to single stimuli of the caudate nucleus which elicited spindles on the anterior sigmoid gyrus. The most marked response pattern was an inhibition of activity in the 150-300 msec period preceding the cortical spindle waves, followed by either bursts of discharges during 2-3 of the waves in the spindle train or, in a few neurons, a cluster of discharges during each spindle wave. Other response patterns included: (1) inhibition of activity preceding the spindle waves; (2) as above, plus a prolonged discharge during the spindle waves; (3) inhibition of activity during the spindle waves; (4) inhibition of activity preceding and during the spindle waves; (5) as above, plus a prolonged discharge at the end of the spindle train; and (6) a prolonged discharge in the period preceding the spindle waves. The finding that various thalamic nuclei differed in their characteristic response patterns during the cortical spindles will be discussed in terms of the different functions performed by these nuclei in the development of spindle activity.

774 EFFECTS OF MEDIUM CATIONS ON ORGANIC ACID TRANSPORT IN ISOLATED GOLDFISH KIDNEY. T. Hoshi and H. Hayashi. Dept. of Physiology, Tohoku Univ. Sch. of Med., Sendai, Japan.

The uptake of phenol red and p-aminohippurate by isolated goldfish kidney was studied under various external ionic conditions. At a fixed Na⁺ concentration, the uptake curve was composed of two components, one linear with the concentration of the acids and the other obeying Michaelis-Menten kinetics. The latter was absolutely dependent on the presence of Na⁺ in the medium, and a graded reduction of the Na⁺ concentration caused a graded increase in the transport Km without changing the Vmax. The Km was found to be a function of the reciprocal of the square of external Na⁺ concentration, suggesting an involvement of a process of activation of the carrier by two Na atoms in this transport. Choline⁺ and K⁺ had no such an activating effect in the absence of Na⁺. Medium Ca⁺⁺ exerted an inhibitory effect on the Na-dependent transport of the acids in its concentration range of 0.2-9.0mM. An increase in the Ca⁺⁺ concentration caused a linear increase in the Km without changing the Vmax. The Na⁺-Ca⁺⁺ antagonism observed in the present study can be explained in terms of competition between 2Na⁺ and Ca⁺⁺ for the carrier of the organic acids.

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MODIFICATIONS OF SWEAT RATE BY CARBON DIOXIDE BREATHING IN MAN . Y. Houdas, M. Bonaventure and A. Sauvage . Lab. of Physiology, Fac. of Medicine, 59. Lille, France .

Inhalation of carbon dioxide appears to elicit a sudorific response in neutral environment or an increase of the sweat flow in hot environment. The total sudoral flow was investigated by continuous recording of the body weight, the subject resting in supine position in a climatic chamber. The subject was breathing air and rested 90 minutes at 40°C (V=.3 m/s and Pwa=10mmHg) to achieve thermal equilibrium. Inhalation of normoxic mixture with 4.5 % of CO2 during 15 minutes produced successive modifications of the sweat rate: first a decrease, then an increase. Finally the sweat rate tended to the control value but presented some oscillations around it. The delay for the increase in sweat flow and the magnitude of the sweat flow variations were different with the subjects. Variations could also be observed in the same subject from one experiment to another. It was concluded that inhalation of carbon dioxide produced disturbances probably at different levels of the thermoregulatory system. However the thermoregulatory system could overcome this non-thermal perturbation at least when the duration of hypercarbia was short.

THE LENGTH AND ORGANIZATION OF PARALLEL FIBERS. J.C. Houk and J.V. Walsh, Department of Physiology, Harvard Medical School, Boston, Mass, U.S.A.

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Parallel fibers in cerebella of cats are currently believed to be 3 mm or less in length and arranged in a staggered array along the longitudinal axis of folia. A reinvestigation of this topic was prompted by Cajal's original claim that parallel fibers coursed the entire width of cerebellar lamellae and by our confirmation of this claim in the turtle cerebellum. Parallel fiber vollies were evoked by stimulation of the surface of the culmen in cats anaesthetized with sodium barbiturate. The amplitude of the volley decreased with distance from the site of stimulation. The amount of attenuation which was due to temporal dispersion was estimated using the progressive widening of the volley as an index of temporal dispersion. We were unable in the vermis to demonstrate significant termination of parallel fibers from distances up to 4 or 5 mm. Beyond this point the parallel fiber volley could not be satisfactorily measured due to its low amplitude and its admixture with Prukinje cell responses. While our results do not allow estimation of the full length of parallel fibers, they do demonstrate that most are longer than 4 mm. This finding has important implications toward the processing of information by Purkinje cells and suggests that cerebella of lower forms may not differ greatly from those of mammals.

HORMONAL REGULATION OF URINE EXCRETION IN THE HEN. B.R. Howard. Agricultural Research Council's Poultry Research Centre, Edinburgh, Scotland.

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The control of urine output in birds is traditionally assumed to be under the control of the supra-optic nucleus of the hypothalamus; this elaborates quantities of arginine vasotocin which are released into the neurohypophyseal blood stream according to prevailing osmotic conditions (Skadhouge, 196h). However, lesions of the supra-optico-hypophyseal tract did not always cause polydoepsia or polyuria. In one hen, complete destruction of the neurohypophysis caused a 50% reduction in fluid intake; urine output fell to unmeasurably low levels and was not raised by intravenous infusion of hypotonic saline. The responses of water-loaded birds to intravenously administered pituitary extracts was studied in adult Brown Leghorn hens. Urine output was unaltered by arginine or lysine vasotocin at physiological levels. Infusion of the saline extract of half a neurohypophysis significantly increased urine output for up to 30 min. This response was mimicked by oxytocin and also by the neurohypophyseal fraction which travelled with oxytocin on a paper chromatogram. It is concluded that the neurohypophysis of the domestic fowl contains a diuretic factor which has certain affinities to oxytocin.

E. Skadhouge: Effects of Unilateral Infusion of Arginine Vasotocin into the Renal Portal Circulation of the Avian Kidney. Acta Endocrinol. (1964). 47, 321-30. 778 POWER OUTPUT OF SWIMMING FISH; THE RELATION BETWEEN THRUST, DRAG AND VELOCITY. J.V. Howarth. Marine Biol. Lab., Plymouth, Devon, U.K.

The power output of a fish swimming at constant speed can be calculated from the hydrodynamic drag or from the thrust generated. Drag has previously been obtained from experiments on dead or inactive fish and thrust can be calculated on the basis of a reactive theory of propulsion from observations on actively swimming fish, but the two sets of figures so obtained are not in agreement. Experiments have been made to try to determine the drag of a fish during active swimming. A spinal dogfish was attached to a drag balance under artificial respiration and propelled through still water while the swimming rhythm was maintained. Amplitude, frequency and wavelength of the swimming action was measured together with water-speed and drag-thrust difference. The swimming effort of the spinal fish was roughly constant. The results showed that at speeds up to twice the cruising swimming speed the drag-thrust difference varied with speed in the expected manner but at higher speeds the drag was less than expected, and often less than that of an inactive fish. The external useful power output at cruising speed was not less than 13 gm.cm.sec. per gm. of muscle at circa 12°C.

779 ULTRAMICROANALYSIS OF pH, P AND CARBONIC ANHYDRASE ACTIVITY AT CALCIFYING SITES IN NORMAL CARTILAGE AS WELL AS EFFECTS OF ACIDOSIS ON LOCAL pH. D.S. Howell and L.A. Cuervo. Dept. of Medicine, Univ. of Miami School of Med., Miami, Fla.

The mechanism by which the [HCO $_3$ -] is elevated in extracellular cartilage fluid (C $_{\rm fl}$) of rat tibial growth plates was investigated. Acetazolamide reduced the [HCO $_3$ -] in C $_{\rm fl}$ to the plasma level. This effect could not be ascribed simply to the generalized acidosis produced by acetazolamide because control rats with a similar degree of acidosis induced by NH Cl maintained the C $_{\rm fl}$ -plasma difference. The distribution of carbonic anhydrase (C.A.) activity in epiphyseal and metaphyseal tissues was determined by microassay. It was found that the enzyme was absent from cartilage but present in significant amounts in surrounding tissues. Finally, the pH - P $_{\rm CO}$ relationship of synthetic lymph to which was added in vitro, cationic proteins bore 2 no resemblance to pH - P $_{\rm CO}$ curves of C $_{\rm c.}$.

The results revealed that C.A. activity present in neighboring structures was probably responsible for the high [HCO₃-] found in C_{f_1} ; It is proposed that epiphyseal capillaries, metaphyseal capillaries or bone cells are involved in secretion of [HCO₃-] at calcifying

sites during metaphyseal growth.....

780 RENAL EXCRETION AFTER MUSCULAR ACTIVITY. O.J.Hrubik. Inst.of Physiology, Med. Faculty, Novi Sad, Yugoslavia.

Muscular activity is known to retard, reduce and delay the excretion of the water load, salts and metabolites within the first few hours. If the amount of muscular activity is small, of short duration and a water load is introduced immediately after, excretion of the same will vary depending on whether the rats in question are "good" or "poor" swimmers, or whether human individuals are active basket-ball players or students not engaging in sports. It is difficult to account for the experimental deviations obtained, which contradict the fact stated in the first sentence, by the most conspicuous cardiovascular adaptation alone.

THE CALORIGENIC EFFECT OF NOREPHINEPHRINE IN NEWBORN RATS. A.C.L. Hsieh, N. Emery and L.D. Carlson. Dept. of Human Physiology, School of Medicine, University of California, Davis, California, U.S.A. 95616.

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The resting oxygen consumption and the response to subcutaneously injected norepine-phrine (NE) has been estimated at 35 C, in newborn rats 1-7 days old. The dose of NE required to elicit a response increased from $12.5~\mu g/kg$ at 1 day to $50~\mu g/kg$ at 7. Doses of 400 and 800 $\mu g/kg$ were toxic at 1 day but were not so at 7 days of age. Maximum responses were obtained with doses of $100~\mu g/kg$ at 1 day and 400 to $800~\mu g/kg$ at 7 days of age. Maximum responses increased with age. This was so even when the response was expressed as a per cent increase over estimated resting levels, or as increase per kg body weight. It is concluded that the sensitivity of rats to NE is highest at birth but decreases during the first week of life. On the other hand, the power of the systems responding to NE increase during the first week of life. Brown fat can be identified in the rat as early as the eighteenth day of fetal life and the newborn animal has fairly large amounts. There may be an increase in brown fat during the first one or two weeks of life in the rat as in the hamster. (This study was supported in part by U.S. Army Contract DADA-17-67-C-7116).

STRUCTURAL SPECIFICITY OF RENAL TUBULAR TRANSPORT OF TRYPTOPHAN DERIVATIVES. K.C. Huang and \underline{Y} .L. Chan. Univ. of Louisville, Med. Sch. Louisville, Kentucky 40202 USA.

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Our previous experiments in dogs have shown a structural specificity in the renal excretion of tyrosine and tryptophan derivatives. In the present investigation, this study was extended using the microperfusion technique of Sonnenberg and Deetjen. Sprague-Dawley rats were anesthetized with "Inactin" 100 mg/Kg i.p. The test amino acid or its derivative and inulin were dissolved in a steady state solution used to perfuse a surface loop of proximal tubule at a rate of 16 nl. min⁻¹. It was found that D-tryptophan, 5-OH-L-tryptophan and 5-OH-tryptamine were nearly completely recovered from the perfusate, indicating that none of the compounds were reabsorbed by the proximal tubule. The permeability coefficient was calculated to be 2.36 x 10-5 cm. sec.⁻¹. In contrast, L-tryptophan was found to be rapidly reabsorbed from the perfusing solution by a mechanism inhibited by L-phenylalanine, but unaffected by sodium azide. Free-flow micropuncture studies with D-tryptophan revealed a TF/Pp-tryp, to TF/P_{In}, ratio in proximal tubular fluid greater than one suggesting tubular secretion, but in final urine samples a ratio less than one was obtained, indicating that after this proximal secretion D-tryptophan undergoes net reabsorption at a site distal to the proximal convoluted tubules. This finding confirms the data obtained from experiments on the renal excretion of tryptophan derivatives in dogs (Am. J. Physiol. 219:1468, 1970). Kinetic studies indicate a tubular maximum for the reabsorption of L-tryptophan. (Supported by grants from NIH AM-2217-13 and NSF GB-8435)

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EFFECT OF ANIONS ON THE ARRHYTHMIAS OF THE CHICKEN EMBRYO HEART. T. F. Huang and G.L.Juang. Dept. of Physiology, Col.Med., Natl. Taiwan Univ., Taipei, Taiwan, Republic of China.

Transmembrane potentials of the ventricle of the isolated heart of chicken embryo aged 8 - 14 days were recorded by the microelectrode technique. The specimen was perfused with the oxygenated Tyrode solution in the muscle chamber of 25 ml at 31°C. The arrhythmias were produced by addition of 0.05 ml of 0.01 % aconitine in vicinity of the specimen. After washing out aconitine, the rapid irregular firing of the specimen persisted. Then the Tyrode solution was replaced by the perfusates in which NaSCN, NaI, NaNO₂ or NaBr substituted for 25, 50 and 100 % of NaCl content in the Tyrode solution. The pattern of the rapid firing of the specimen in various perfusates was recorded at some intervals during 60 min perfusion period. Effectiveness of anions to depress the rapid firing was in the order SCN > I > NO₂ > Br . It is concluded that alteration in chloride permeability participates in the process of the arrhythmias, and that other foreign anions can affect the arrhythmias.

784 Role of Cl⁻ ion in active Na⁺ transport in frog skin. E. G. Huf. Dept. of Physiology, Virginia Commonwealth University. Richmond, Virginia USA.

Ferreira (1968) found that in short-circuited frog skins net Na transport (J_n) is greater when the skins are bathed in Cl-, instead of SO $_4^2$ -Ringer's. The present work confirms this observation and gives evidence for differential Cl-reffects on the two sides of the skin (R.esc.). Patterns of behavior of current (SCC), PD, conductance, Na and Cl- influx and outflux upon sequential changes of SO $_4^2$ - ("S") and Cl- Ringer's ("Cl") on both sides (o and i) of paired skins will be presented. Solutions (mfq/l): S-Ringer's, [Na+]=104; [K+]=3; [SO $_4^2$ -]=100; [Cl-]=4; [HCO $_3^2$ -]=3, mannitol (M) to give 200 mosm., pH=7.5. Cl-Ringer's, as above, except [Cl-]=100, [SO $_4^2$ -]=4, no M, 200 mosm. Results: 1) SoCl $_1^2$, increase in Jn. (control SoS $_1^2$). Same result with M-free So, 67 mM NaCl $_1^2$, 135 mosm. 2) CloS $_1^2$, increase, or decrease in Jn (or SCC), varying with skins. (control SoS $_1^2$). 3) CloCl $_1^2$, decrease in Jn (control SoCl $_1^2$). In all cases little change in Na+ outflux. Sum of Na+, Cl- fluxes equalled SCC. A weak inward Cl- pump is demonstrable with skins in SoS $_1^2$. Conclusions: Separate mechanisms of actions of Cl- at the inside and outside determine the net rate of transpithelial Na+ transport. The inside effect may be the result of epithelial swelling (increase in number of transport sites?). The outside effect suggests that entry of Na+ into the skin involves interaction of Na+ with a skin structure (str. corn.?) which facilitates or depresses Na+ entry depending on [Cl-] $_0$. Support of Na+ entry by a weak Cl- pump cannot be excluded. (NIH Grant GM 03545)

785 THE EFFECT OF BUFOTENINE ON CEREBELLAR DISFACILITATION IN CATS. Ronald D. Huffman. Dept. of Anatomy and Pharmacology, Univ. Texas Med. Sch., San Antonio, Texas 78229, USA.

Intravenous injection of bufotenine (5.0 mg/kg) in monkeys has been reported to produce a prone position in which these animals cannot walk or climb. This is followed by a period of marked ataxia and heightened tendon reflexes. In humans, nystagmus has been reported. These observations suggest that bufotenine may be acting at the level of the cerebellum to alter normal cerebellar somatomotor control. Since the entire outflow from the cerebellar cortex (Purkinje/neurons) is inhibitory in function and since some of the functional observations suggest a reduction of inhibitory input to spinal motoneurons, this study was designed to investigate the effect of bufotenine on cerebellar inhibition (disfacilitation) of the segmental (quadriceps and biceps-semitendinosus) monosynaptic action potentials. Midcollicular decerebrate cats were used in these experiments. Surface stimulation of the vermis of the anterior lobe of the cerebellum with bipolar silver ball electrodes was used to induce the disfacilitation of the segmental potentials. Intravenous injections of bufotenine (0.25-0.5 mg/kg) markedly reduced or completely eliminated the cerebellar disfacilitation of both segmental potentials; the depression of this disfacilitation lasted approximately 50 min. The segmental potentials were unaffected or slightly reduced by these same doses; this effect, however, was quite variable. Direct inhibition of the biceps monosynaptic potentials induced by stimulation of the antagonistic quadriceps nerve was unaffected by bufotenine (2.0 mg/kg). Reticular inhibition was unaffected or only slightly reduced with doses of bufotenine as large as 1.5 mg/kg.

786 RELATION OF BRONCHIAL LENGTH TO LUNG VOLUME. J.M.B. Hughes, B.J.B. Grant, H. Jones, J. Mead. Dept. of Med., Royal Postgraduate Med. Sch., London W.12, England, and Dept. of Physiology Harvard Sch. of Public Health, Boston, U.S.A.

We have measured bronchial length in human and dog lungs with a stereo x-ray pair technique after outlining airways with tantalum dust. At lung volumes in excised dog lungs greater than 30-3% of maximum, all bronchial lengths changed proportionately with the cube root of absolute lung volume. There was very little further change of length however at lower lung volumes. At maximum inflation bronchial segments were about 60% longer than their resting length. Dissected bronchi over the same range of distending pressure lengthen less (at most 30%). The greater bronchial length in situ suggests that airways are subjected to longitudinal stresses in excess of transpulmonary pressure. In the intact dog, we extended the bronchial tree without changing lung volume by pulling on a rod with three radial hooks at its end which had been passed down the trachea and hooked into an intrapulmonary bronchus. At functional residual capacity a 10% change of bronchial length required forces equivalent to local pressures in excess of 100cmH₂O (axial force/cross sectional area at site of attachment). Thus the shear stresses developed by lung tissue appear to confer a high degree of longitudinal stability on bronchi. This may be of importance in dynamic events such as coughing. The internal shear which develops in airways because of the drag of flowing gas may be opposed by an external shear from lung tissue.

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NEURONAL MECHANISMS OF VAGAL RESPIRATORY REFLEXES IN THE BRAINSTEM OF THE CAT. T. Hukuhara Jr. Dept. of Pharmacol., Sch. of Med., Univ. of Tokyo, Tokyo, Japan.

In order to elucidate the neuronal organization of afferent vagal pathways to bulbar respiratory neurons the unit activity was recorded in Flaxedilized and vagotomized cats. The cervical vagus nerve was stimulated at frequencies ranging from 5-320 Hz. Both the respiratory unitary discharge and phrenic discharge were facilitated by weak stimulation at low-frequency and inhibited at high-frequency. The critical frequency at which a reversal of effect revealed ranged from 40-80 Hz in the majority of neurons. The reversal was caused after the brainstem was transected at the ponto-medullary junction. Responses of respiratory neurons to single shocks were examined in order more specifically to analyze the neuronal mechanisms of the reversal. A total of 123 neurons were under investigation. The orthodromic response was observed in 20 cases including inspiratory, expiratory and another broader group. These neurons were scattered throughout the lateral regions of the bulbar reticular formation. The latency ranged from 1.7-17.0msec and the range of the frequency following was 10-50 Hz. The rest of neurons(103 cases)did not respond. The highfrequency stimulation which abolished the orthodromic response of neurons caused simultaneously an inhibitory effect in both the phrenic and unitary discharge of other neurons. Pentobarbital(1-5 mg/kg i.v.)abolished the orthodromic response of neurons as well as the facilitatory effect of both discharges by low-frequency stimulation. The frequencydependence of the facilitatory effect would relate to the limited ability of respiratory neurons to follow orthodromically increasing frequencies of vagal stimulation.

EFFECT OF CORTICAL SPREADING DEPRESSION ON BEHAVIOR EXICITED BY ELECTRIC HYPOTHALAMIC STIMULATION. J.P. Huston. Institute of Physiology, Czechoslovak Academy of Sciences, Prague, Czechoslovakia.

Eating and drinking were elicited in rats by stimulating electrically in lateral hypothalamic areas. Single waves of unilateral cortical spreading depression (CSD) were administered by injecting 6% KCl through cannulae chronically implanted over the occipital and frontal cortices. When the hypothalamus was stimulated with current levels at threshold for eliciting eating or drinking, a wave of CSD temporarily eliminated all elicited consummatory behavior. At higher current levels, however, a wave of depression merely increased the latencies of the elicited behaviors, suggesting that the spreading depression decreased the excitability of the hypothalamus. Cortical spreading depression can also modify the type of behavior elicited by hypothalamic stimulation. For instance, in one animal stimulation at 60µÅ elicited drinking, but at 90µÅ elicited primarily eating. During a wave of CSD 90µÅ temporarily elicited only drinking. Such data again suggest that the CSD caused an increase in threshold of hypothalamic activation.

SPIKE TO ECCENTRICITY FUNCTION ACROSS A RETINAL GANGLION CELL RECEPTIVE FIELD TO FOCUSED AND BLURRED IMAGERY. Hisako Ikeda and *Richard M.Hill. Res. Dept. of Ophthalmology, Royal College of Surgeons of England, London, and *Col. of Optometry, The Ohio State University, Columbus, Ohio, U.S.A.

Using focused and defocused stimuli, both suprathreshold and threshold responses of very local areas within ganglion cell receptive fields were measured. The effects of myopic and hyperopic errors on the responses of these cells included a functional change of field radius (due partly to scattered light, estimated by photo-densitometry methods), a relative shift of central and peripheral thresholds across the field and a rapid decrease of the spike to eccentricity ratio as the stimulus deviated from the field axis. Three neurophysiological criteria of functional emmetropia were formulated and compared with objective measurements of refractive error.

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790 PACEMAKING ACTION OF A NEURON INDUCED BY A SINGLE GENE MUTATION IN <u>DROSOPHILA MELANOGASTER</u>.
K. Ikeda and W. D. Kaplan, City of Hope National Medical Center, Duarte, Calif. 91010, USA.

The intracellular recording of neural activities from a neuron of mutant Drosophila shows a pacemaking action derived from a single gene mutation. Previous work on Drosophila HklP shows the following: HklP has rhythmic leg-shaking action under ether anesthetization. The underlying neural mechanism is in the endogenous rhythmic activity of neurons in the motor regions of the thoracic ganglion. Motor neurons lack autogenic rhythmicity but are driven by interneurons; their output pattern is dependent on the activity of those interneurons, suggesting they are the pacemakers expressing the genetic change. At least one interneuron of this type is in each of three pairs of motor regions; interneurons in the separate regions operate independently. The pacemaking action of these interneurons are investigated in the present study. The amplitude, duration, and periodicity of the pacemaker potential are the main factors determining the pattern of impulse sequence. Another factor is also characteristic of this neuron. The soma membrane shows pacemaker potential but appears not to fire impulses, which are initiated at some portion of the axon. The site of initiation gradually shifts along the axon; this shift affects the pattern of impulses even when the pacemaking activity pattern at the soma is unchanged. When the site is close to the soma, the impulse pattern is a continuous discharge of high frequency with fluctuation depending on the phase of pacemaker potential; when it is far from the soma, the impulse pattern can be intermittent.

791 THE RESPONSE OF MEDULLARY RETICULAR NEURONES TO ELECTRICAL STIMULATION TO THE CHEMO-RECEPTOR TRIGGER ZONE IN AREA POSTREMA OF THE DOG. M. IKEDA and Y. IWASE. Dept. of Physiology, Kyoto Prefectural Univ. of Med., Kyoto, Japan.

Vomiting was induced by the electrical stimulation of chemoreceptor trigger zone (CTZ) in area postrema. Activities of reticular neurones were investigated in response to single and repetitive stimuli in order to analyze the nature of the "vomiting center".

(1) Responses of reticular neurones to single shock CTZ stimulation were grouped into responsive (excitatory and inhibitory) and indifferent types. (2) Over 40% of neurones in the dorsal portion of the nucleus reticularis parvocellularis near the CTZ was found to be responsive. (3) Relative incidence of responsive neurones increased after the administration of emetics (apomorphine and copper sulfate) and decreased after the administration of antiemetics (metoclopramide and sulpiride). These results seem to indicate that reticular neurones within the dorsal part of the nucleus reticularis parvocellularis adjacent to the nucleus of the solitary tract play some role in the central nervous mechanism of vomiting reflex.

792 QUANTITATIVE ANALYSIS OF THE INITIAL SODIUM CURRENT IN THE TWITCH SKELETAL MUSCLE FIBRE OF THE FROG. M.Ildefonse, O.Rougier and G.Roy. Lab. of animal Physiology, CNRS-ERA III, 86 Poitiers, France and Univ. of Montreal, Canada.

Records, with a double voltage-clamp sucrose-gap technique, of the rapid initial current of a twitch skeletal muscle fibre isolated from the semi-tendinous of the frog, have allowed us to make a quantitative study of this current, according to the theory of $\frac{\text{Hodgkin}}{\text{Adding}}$ and Huxley. Because of the difficulty of defining a component of leak current in skeletal muscle (anomalous rectification and a high chloride permeability), the net sodium current has been obtained by substracting the current observed after the action of TTX from the whole membrane current. The sodium conductance as defined by the authors does not seem to be able to account for the permeability of this membrane to sodium ions; so, the equation of permeability according to the constant field theory was used. The inactivation process (h_{∞} -potential and τ_h -potential curves) has been established experimentally. A curve-fitting method has permitted to determine the "m" activation process. The parameters values found for the two systems are compared to those given by $\frac{Adrian et all}{Adrian}$ (1970); the differences might be partly explained by the difference in the temperatures at which the experiments were performed (23°C in our experiments instead of 3°C in theirs). The results are also considered in regard to the model proposed by $\frac{Roy}{BO}$ (1969).

THE EFFECT OF DIFFERENT Ca⁺⁺AND Mg⁺⁺CONCENTRATIONS ON THE ACETYL—CHOLINE RELEASE AND SYNTHESIS IN THE BRAIN CORTEX OF THE RAT.P.Illés, E.S.Vizi, G.Somogyi and J.Knoll.Dept.of Pharmacology, Semmelwels Medical University, Budapest, Hungary.

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University, Budapest, Hungary.

The acetylcholine /ACh/ release from brain cortex slices of the rat has been studied under different ionic conditions. Cortex slice was bathed in Krebs solution /2 ml/ containing eserine sulphate in a concentration of 2 ug/ml. The resting release /2,46 ng/g.min/ was increased to 9.71 ng/g.min, when the /K/ concentration was increased from 5,9 to 24mM. The effect of different external Ca concentrations /0 - 2,5 + 4,3 - 10,1 mM/was investigated both on resting and potassium augmented ACh release at different Mg concentrations /0 - 1,2 - 9,2 mM/. Since the rate of synthesis might have some influence on ACh release, the effect of ionic changes on ACh synthesis rate was determined. The resting synthesis proved to be as high as 0,47 ug/g.2 h. Neither omission, nor increase of Ca++ had considerable effect on the synthesis. Absence of Mg augmented, whereas Mg-excess /9.2 mM/ abolished it. In order to remove the tissue calcium, 1 mM EDTA was administered; release and synthesis was also measured under this condition.

CIRCULATORY CHANGES FOLLOWING ADRENALECTOMY IN THE RAT. F.J. Imms and R.L.B. Neame. Sherrington School of Physiology, St. Thomas's Hospital, London, S.E.l., England.

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Rats were adrenalectomised under ether anaesthesia. Following recovery they were given 0.9% NaCl soln. to drink. One to seven days after adrenalectomy (adrex) they were anaesthetised with pentobarbitone Na and cardiac output (CO) and arterial blood pressure (ABP) recorded. CO was determined by a thermal dilution technique. A cold stimulus (0.1 ml of 0.9% NaCl soln. at room T) was injected into the right atrium. Passage of cooled blood through the circulation was monitored by a sensitive thermistor placed in the arch of the aorta. The mean ($^{\pm}$ SEM) CO for intact animals was 24.5 $^{\pm}$ 2.5 ml/100 g body weight/min. One day after adrex CO had fallen to 16.6 $^{\pm}$ 2.6 (P<0.025), but by the third post-operative day it was normal. The mean ABP of the controls was 119.4 $^{\pm}$ 5.2 mm Hg. ABP was 104 $^{\pm}$ 4.9 (P<0.025) one day after adrex, and remained lower than normal seven days after operation. One day after adrex heart rate (HR) had increased from 369 $^{\pm}$ 15.1 to 443 $^{\pm}$ 19.8 (P<0.01), and remained high 3 days after adrex. Stroke volume (SV) of theleft ventricle of control rats was 0.281 $^{\pm}$ 0.026 ml. This fell to 0.158 $^{\pm}$ 0.032 (P<0.01) one day after adrex, and was still reduced 7 days after operation. Sham-adrex did not affect CO, ABP, HR and SV. These observations support the hypothesis that the contractile force of the heart is impaired after adrex.

ANALYSIS OF MUSCLE SERVO LOOP. G.F. Inbar, Dept. of Electrical Engineering, Israel Inst. of Technology, Haifa, Israel.

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The function of the muscle spindle (MS) in muscle control has been analyzed by Merton (1) His length follow-up servo model is analyzed here, in view of experiments carried out on spinalized frogs. Single MS afferent outflow, from either the sartorious or gastrac-nimious muscles, was recorded from the dorsal root ganglion, while the efferent-afferent muscle loop was intact. The same MS outflow was recorded again after opening the loop, by cutting all the dorsal root filaments from the muscle understudy. Both open and closed loop measurements were carried out while the muscle was being stretched mechanically, and its tension recorded. The closed loop results show smoother frequency response and lack of dead zones. The loop gain was found to be very low, less than 2.0, both for the tension and the MS's own loop. It is suggested that this low gain does not conform with the servo assisted muscle control concepts.

(1) Merton, P.A., in The Spinal Cord, Ciba Foundation Symposium, 1953.

796 EXCITATORY AND INHIBITORY TRANSCALLOSAL EFFECTS RECORDED FROM SI CORTICAL NEURONES. G.Innocenti and T. Manzoni. Institute of Human Physiology, Univ. of Catania, Catania, Italy.

The present experiments were performed in order to analyze the transcommissural reactivity of $S_{\rm I}$ cortical neurones to contralateral cortex stimulation $(S_{\rm I},\,S_{\rm II})$ and anterior lateral associative) and, further, to correlate each other the pattern of reactivity to the commissural and peripheral inputs. During electrophysiological experiments in chloralose-anaesthetized, curarized cats (expiratory pCO_2 continuosly monitored),117 $S_{\rm I}$ neurones have been thus far investigated with glass micropipettes and intracellular records were obtained in a good proportion of them. Transcommissural effects, both excitatory and inhibitory in sign, were observed in 11 lemniscal and 21 extralemniscal units (17% and 65% of their respective pools).By intracellular records, the effects were seen to consist of: (i) slow, often long-lasting (up to 70 msec) and graded,depolarizing potentials that can bring the cell to single and/or multiple firing, followed by variable appearance of hyperpolarization; (ii) polarizing potentials (up to 140 msec; peack amplitude 3-6 mV) without preceding depolarization, during which units exhibited unresponsiveness to peripheral impulses. The effects described were almost exclusively observed following contralateral $S_{\rm I}$ stimulation and their latencies are consistent with the callosal mediation.

797 SIMULTANEOUS BLOOD PRESSURE AND VELOCITY MEASUREMENTS IN MAMMALIAN MICROVESSELS. M. Intaglietta. Dept. of AMES-Bioengineering, University of California, San Diego, La Jolla, California 92037. U.S.A.

Pressure and red blood cell velocity was measured simultaneously in microvessels of 15 μ diameter and larger in the cat omentum. Pressures were measured directly by a resistance null-balance, feedback method, and velocities were measured simultaneously and on-line by continuous crosscorrelation of signals produced by the image of the blood vessel projected unto two adjacent photodetectors. Crosscorrelation as a function of time delay between systemic and microscopic data, allowed to reconstruct wave forms and determine phase relationships. It was found that the omental micro-vasculature behaves as a highly compliant system, where pulsations persist through venous microvessels, up to 80μ diameter.

798 REGIONAL SYMPATHETIC ACTIVITY DURING HYPOXIA AND HYPERCAPNIA. M. Iriki, K. Pleschka, O.-E. Walther, E. Simon. W.G. Kerckhoff-Institut der Max-Planck-Gesellschaft, Bad Nauheim, Germany.

Gesellschaft, Bad Nauheim, Germany.

Increase of skin blood flow with simultaneous decrease of visceral blood flow during moderate asphyxia (1) corresponds to antagonistic changes of regional sympathetic activity, while during severe asphyxia sympathetic activity increases in both regions (2). The contributions of hypoxia and hypercapnia to these responses were investigated in 15 rabbits. — Under sodium pentobarbital, succinyl choline and artificial ventilation with gas mixtures of various O₂ and CO₂ contents, the discharges of a postganglionic nerve twig accompanying the retroauricular artery (cutaneous sympathetic activity = CSA) and of a splanchnic nerve branch (visceral sympathetic activity = VSA) were recorded. PaO₂, PaCO₂ and pH were measured. — During moderate hypoxia (PaO₂ 27.2 - 2.8 Torr; n = 8) CSA decreased, corresponding to increased skin blood flow (3), while VSA increased. Severe hypoxia (PaO₂ 16.4 - 2.0 Torr; n = 5) increased both CSA and VSA. Hypercapnia (PaCO₂ 59.3 - 5.4 Torr; n = 8) had no substantial effects. Thus, the regional sympathetic responses to asphyxia are caused mainly by hypoxia.

(1) A. Dastre, J.-P. Morat: Arch. Physiol. norm. path. 16: 1, 1884. (2) M. Iriki, O.-E. Walther, K. Pleschka, E. Simon: Pflügers Arch. 322: 167, 1971. (3) J.P. Chalmers, P.I. Korner: J. Physiol. (Lond.) 184: 685, 1966

INCREASE OF MEMBRANE CONDUCTANCE BY 5 HT IN THE HEART MUSCLES OF BIVALVE MOLLUSCS. H. Irisawa, L. Wilkins and M. J. Greenberg. Physiologisches Institut, Universitat Bern, Switzerland and Department of Biological Sciences, Florida State University, Tallahassee 32306, U.S.A.

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Using the double sucrose gap method, constant current was applied to the heart muscle of Modiolus demissus and Mytilus edulis. Both acetylcholine (ACh) and 5-hydroxytryptamine (5HT) inhibited the spontaneous beating of Modiolus hearts, while slightly hyperpolarizing the cell membrane. The ACh hyperpolarization was accompanied by an increase in membrane conductance; but the conductance change with 5HT was small. Both ACh and 5HT excited the beating of the Mytilus heart; a concomitant membrane depolarization occurred. Again, the increase of membrane conductance by ACh is more prominent than that of 5HT. Although changes in membrane conductance effected by 5HT were slight, the critical firing level was markedly increased. The 5HT inhibition of rhythmical activity was not abolished, either by the replacement of Cl with propionate, or by replacement of Na⁺ with Tris chloride; still, the conductance change was reduced to a negligible degree. The reversal potential of ACh in Modiolus, was slightly lower than the resting potential; the reversal potential of SHT was even lower than that of ACh. Thus, different mechanisms are involved in the actions of these two neurotransmitters, in molluscs. (Supported by USPH Grant HE-09283.)

EFFECTS OF NITRITES ON ARTERIAL COLLATERAL VESSELS. J. Iriuchijima Dept. of Physiology, Faculty of Medicine, University of Tokyo, Japan.

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In dogs anesthetized with pentobarbital, resistances of the collateral flow channels of the common carotid and femoral arteries were calculated by measuring flow through the arteries as well as pressures proximal and distal to the site of arterial occlusion. When the common carotid artery was occluder, collateral resistance gradually decreased in about 30 sec, from initial collateral resistance (ICR) of 0.84 ± 0.41 mmHg/ml/min (mean with SD from 6 dogs) to steady state collateral resistance (SCR) of 0.52 ± 0.27 (significant at P<0.01). Intravenous injection of a long-active nitrite, N-ethoxy-carbonyl-3-morpholino-sydnonimine (SIN 10), at a dose of 1 mg/kg, diminished ICR (-38 $\pm20\%$, n=6, P<0.01, 15 min after administration) but not SCR, thus ICR approaching SCR. This effect was maximum from 15 to 60 min after the intravenous injection. ICR of the femoral artery was also decreased by SIN 10 (-49 $\pm5\%$, n=6, significant at P<0.001). Nitroglycerin had a similar effect of dilating the collateral vessels for both arteries, though its effect was more evanescent in the time course and almost disappeared 5 min after injection. It is concluded that nitrites dilate almost the same collateral vasculature which would gradually open during arterial occlusion.

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Istanbul.

Verschiedene Narkotika verursachen beim Tier zum Teil erhebliche Veränderungen im EKG gegenüber dem Wachzustand. Veränderungen der Q-, R- und S-Werte, Verkürzung der QRS-Zeit (Urethan), Verlangsamung derselben unter Luminal, Negativierung der T-Zacke, Veränderungen der Q- und T-Zeit. Beim Hund: Q-Voltage maximal, R-Voltage 1,18-1,05, S-Voltage 0,04-0,07,QRS-Zeit 6,67-0,04,QT-Zeit 0,22-0,18. Bei der Katze: Unter Urethan Q vergrößert, unter Pen-

VERGLEICHENDE EKG UNTERSUCHUNGEN AN LABORTIEREN IN VERSCHIEDENEN NARKOSEN.

Irmak, Sadi. Department of Physiology, Faculty of Medicine, University of

tothal P-Voltage minimal. Beim Meerschweinchen:Unter Luminal P-Zeit verkürzt,unter Nembutal P- und R-Voltage maximal.Bei allen Tieren unter Nembutal Pentothal und Luminal Verflachung der T-Zacke. Wenn es auch vorläufig nicht möglich erscheint,alle diese Veränderungen auf eine einheitliche Ursache zurückzuführen,neigen wir doch zur Annahme,daß die Tonusveränderungen im Neurovegetativen System,welche im Narkosezustand auftreten,dabei eine maßgebliche Rolle spielen.Die Veränderungen in der Tätigkeit des Reizleitungssystems des Herzens während der Narkose scheinen zu dominieren. Es kann

aber auch die Arbeitsmuskulatur des Herzens nicht ganz unbeteiligt bleiben, wie die Veränderungen im Endteil des EKG zeigen.

802 EFFECT OF CHANGES IN PERITUBULAR FLUID pH ON THE TRANSTUBULAR POTENTIAL OF ISOLATED AND PERFUSED CORTICAL COLLECTING DUCTS OF RABBIT KIDNEY.

L.C. Isaacson and R.J. Douglas, Department of Physiology, Medical School, University of Cape Town South Africa.

L.C. Isaacson and R.J. Douglas, Department of Physiology, Medical School, University of Cape Town, South Africa.

Transtubular potential difference in the far distal nephron is thought to be a controlling factor in the urinary excretion of H⁺. We have monitored transtubular potentials (PD) over several hours while inducing step changes in pH of the peritubular fluid. PD was measured via an intraluminal pipet inserted several hundred microns lengthwise down the tubule. We have observed that: (1) Lowering bathing fluid pH in the range 7.3 to 6.1 elicits an increase in luminal negativity. In one instance a drop in pH from 7.3 to 7.2 increased the transtubular PD from 23 to 30 mV. (2) Raising the pH produced the opposite effect.

(3) These changes were reversible. (4) The above effects were independent of luminal fluid pH (4.8 to 7.3). (5) Lowering the pH of the bathing fluid still further to pH 5 caused a fall in PD; this was partially reversed on raising the pH to 6.1.

These observations suggest that H concentration in the peritubular fluid might itself be the factor governing H excretion, via an effect on

transtubular PD.

803 INHIBITORY EFFERENT INNERVATION TO THE CHEMORECEPTOR OF THE CAROTID LABYRINTH OF THE TOAD. K.Ishii & K.Ishii. Dept. of Physiology, Fukushima Med. Col., Fukushima, Japan.

The physiological evidence of the efferent innervation to the chemoreceptor was sought in the carotid labyrinth of the toad. A few-fibre chemosensory preparation was splitted from the glossopharyngeal nerve at its peripheral cut end, and the rest part of the nerve was stimulated electrically. The stimulation reduced remarkably the chemosensory discharge on this nerve strand. To seek the derivation of these inhibitory fibres a few-fibre preparation was peeled from the intact glossopharyngeal nerve, and the sympathetic nerve and the vagus group root were stimulated respectively. The stimulation of sympathetic nerve was predominantly effective on provoking the inhibition; the sympathetic stimulation provoked the inhibitory effect in ten of seventeen preparations. In three of these ten the vagus group root stimulation brought about the inhibitory effect, while the sympathetic did not. In the other six no remarkable effect was obtained by both stimulations. It may be concluded that the activity of chemoreceptor cell is controlled by efferent nerves mainly via the sympathetic in toads.

THE EFFECT OF BETA ADRENERGIC BLOCKADE USING SOTALOL (MJ1999) ON LEFT VENTRICULAR FUNCTION IN CONSCIOUS INSTRUMENTED DOGS. E. Ison-Franklin, F. Kraft-Hunter, and E. W. Hawthorne. Dept. of Physiology, Col. of Med., Howard Univ., Washington, D.C., U.S.A.

Dogs were instrumented during sterile surgery to permit simultaneous monitoring of left ventricular internal diameter, left ventricular pressure, aortic pressure and left atrial pressure. All dogs were studied in the conscious state 28 to 30 days post-operative. Following adrenergic blockade with Sotalol (MJ1999), administration of a test dose of isoproterenol, 0.5 mg i.v./kg body weight, produced no change in peak dP/dt, although peak systolic ventricular pressure was elevated. Ventricular end-diastolic diameter and volume were increased while end-systolic diameter and volume remain unchanged. Increase in heart rate in response to isoproterenol persisted following blockade. These data demonstrate an ability of this blocking agent to selectively prevent the sympathetic responses of ventricular myocardial function to isoproterenol without affecting the heart rate response. The heart produced a greater stroke work from a larger end-diastolic size following blockade. Atrial and ventricular end-diastolic pressures during blockade were increased. The basis for these elevations in pressure is not apparent from these data.

EFFECT OF EXERCISE AND EPINEPHRINE (E) ON THE CARBOHYDRATE METABOLISM OF METHYLPREDNIS-OLONE (MP) TREATED DOGS. B. Issekutz, Jr., and M. Allen. Dept. of Physiology, Dalhousie University, Halifax, N.S., Canada.

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Dogs with indwelling arterial and venous catheters ran on a treadmill (15% slope, 100 m/min). 2-t-glucose and 14C-lactate were infused at a constant rate. Hepatic glucose output, lactate turnover and gluconeogenesis from lactate were measured. After 48 hours fasting in normal dogs, the rate of hepatic glucose output increased during exercise about 2-3 fold, the blood glucose decreased and, until exhaustion, a total of about 4 g glucose/100 g liver was produced. After 2-3 days treatment with MP, exercise had a tendency to increase the blood sugar, glucose turnover was more than twice as high as before treatment, the onset of exhaustion was considerably delayed and a total of 12-20 g glucose/100 g liver was produced, while only 7-9% of it was derived from lactate. In similar experiments on resting dogs the effect of E infusion on the glucose production and on gluconeogenesis from lactate were greatly potentiated by MP. It is concluded that the duration of exercise depends on the initial glycogen content of the liver and that the pronounced synergism between the glucocorticoid and epinephrine is responsible for the high rate of glucose turnover in the MP treated animal.

Supported by the Medical Research Council of Canada.

FEEDFORWARD AND FEEDBACK PATHWAYS OF THE VENTROBASAL THALAMIC COMPLEX IN CATS. Y. Iwamura and W. A. Spencer, Dept. of Physiol., NYU Med. Ctr. and PHRI, New York, N.Y. 10016 USA.

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Selective antidromic activation of thalamo-cortical fibers of the ventro-basal complex in anaesthetized cats following chronic somatosensory decortication revealed intracellularly recorded recurrent EPSPs in addition to the well-known recurrent IPSPs. latency measurements of antidromic spikes of TCR cells and of recurrent IPSPs disclosed a minimum latency difference of 1.3 msec. Since this is no shorter than the minimum latency differential between EPSP and IPSP onset from peripheral cutaneous nerve stimulation, it suggests that a feedforward inhibitory pathway operates in addition to the feedback system. Sequentially spaced punctate skin stimuli were used to determine the distribution gradients of excitatory and inhibitory synaptic actions within the receptive fields of TCR cells. IPSP amplitude was greatest at the center of the field where excitation was maximum; both excitation and inhibition dropped off toward the receptive field periphery in similar fashion. True postsynaptic inhibitory surround action was rarely seen in intracellular recordings. In line with these observations, extracellular unitary analysis showed considerable similarity of antidromically identified TCR cell and presumed interneuron receptive field properties, although a few interneurons had especially large fields and showed long burst responses. (Supported by USPHS Grant #NS-09361).

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SODIUM AND CALCIUM SPIKE INITIATION IN A SECRETORY NEURON OF CRAYFISH. S. Iwasaki and Y. Satow. Dept. of Physiology, Univ. of Tokyo and Tokyo Med. Col., Tokyo, Japan

Electrical activities in the soma and axon of a crayfish secretory neuron (X-organ) were investigated with glass microelectrodes. In Na-free or TTX medium, injected current initiated soma membrane action potentials whose amplitude was (Ca^{++}) dependent. In low (Ca^{++}) medium, soma spike amplitude was (Na^{+}) dependent. In normal medium, action potentials propagated in one to one fashion down the axon to the sinus gland, but with application of TTX or Na-free medium, the propagated action potentials of the axon disappeared within one minute while the soma spike remained. It can thus be deduced that the action potential mechanism in the X-organ soma involves two ionic systems, Ca and Na, in parallel, while the action potential mechanism of the axon involves only one ionic system. In Na-free or TTX medium, calcium spikes were investigated by substitution of Sr or Ba for Ca; spike initiation was still possible. However, if Mg or Mn was added to the normal medium or substituted for Ca, spike initiation was antagonized or blocked.

808 EFFECTS OF ACUTE INSULIN DEFICIENCY IN NEPHRECTOMIZED RATS. P.B. Iynedjian and G. Peters. (Inst. pharmacol., Univ. of Lausanne, Switzerland)

In rats nephrectomized or sham-operated 14 hrs earlier, acute insulin deficiency was induced by an intraacrtic injection of 2 ml guinea-pig antinsulin serum (A.I.S.) neutralizing about 1.5 unit insulin per ml; a second 2 ml A.I.S. injection was given 1.5 hr later. The increases in plasma glucose level determined in the nephrectomized, respectively the control animals, were as follows: at .75 hr after the first A.I.S. injection, 49 ± 5 mg per 100 ml, respectively 118 \pm 12; at 1.5 hr, 86 \pm 7, respectively 177 \pm 11; at 2.5 hrs, 125 \pm 14, respectively 180 \pm 10; at 3.5 hrs, 180 \pm 15, respectively 195 \pm 11. These results show that the increase in blood sugar level after A.I.S. injection is much slower in nephrectomized rats than in controls; the difference between the two groups remained statistically significant until 2.5 hrs after the first A.I.S. injection. This difference is apparently not due to the suppression of the excretory function of the kidneys, as indicated by experiments with rats whose ureters were ligated.

(Supported by Fonds National Suisse, R. Sci., Grand NB-5316.3).

809 INTRACELLULAR pH, H ION FLUX AND H ION PERMEABILITY COEFFICIENT IN BULLFROG TOE MUSCLE. Kenneth T. Izutsu, Dept. of Physiology, Univ. of Washington, Seattle, WA, USA.

Intracellular pH of toe muscles (flexor IV) from Rana catesbeiana was estimated in vitro using the DMO technique. Under control conditions (CO $_2$ concentration of 5% and extracellular bicarbonate ion concentration ([HCO $_3$] $_o$) of 24 mM), pH $_1$ is 7.16 \pm 0.01 (S.D.). This value is constant for incubation periods of from 15 minutes to 10 hours. pH $_1$ is affected by changes in PCO $_2$ and [HCO $_3$] $_o$. At a given PCO $_2$, decreasing the [HCO $_3$] $_o$ is more effective in lowering pH $_1$ than increasing the [HCO $_3$] $_o$ is in increasing pH $_1$. The decrease in pH $_1$ following a decrease in [HCO $_3$] $_o$ is exponential with a time constant of 2.3 hours. On the assumption that this decrease is due to H+ movement across the membrane, a H+ flux of $_1$ 0-13 moles/cm $_2$ 0 sec may be calculated. The corresponding H+ permeability coefficient is $_1$ 0-3cm/sec. 1% of the total power available from respiration would be required to maintain an equal and opposite active flux.

THE CONTRIBUTION OF THE DORSAL COLUMNS IN RELAYING CUTANEOUS INFORMATION TO THE SOMATOSENSORY CORTICAL AREAS. S.J. Jabbur, S.F. Atweh and V.T. Topjian, Dept. of Physiol., American University of Beirut, Lebanon.

Evoked gross potentials and single unit responses in the somatosensory cortical areas were studied in anesthetized and paralyzed cats following electrical stimulation of the paws and the dorsal columns (at C4 level). Electrical stimulation of the contralateral forepaw and contralateral dorsal column produced nearly identical potentials in the somatosensory cortical area I (SI). When a gross potential was evoked in SI to ipsilateral forepaw stimulation, a similar correlation was observed with ipsilateral dorsal column stimulation. Nearly all single units responses in SI driven by cutaneous stimulation were also driven by stimulation of the corresponding dorsal column. Similar correlations were observed in somatosensory cortical area II (SII). The above correlations applied to all units irrespective of their submodality, peripheral field size or frequency following behavior. Care was taken to confine the electrical stimulus to the dorsal columns (Fed. Proc., 1969, 28: 396). Our data suggest the need for reevaluation of some current physiological definitions of a dorsal column-lemniscal neuron along the somatosensory path to the cerebral cortex. (Supported by the American University of Beirut).

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SYNCHRONIZED NEURONAL ACTIVITY OF A CIRCADIAN RHYTHM. Jon W. Jacklet. Dept. Biol. Sci. State University New York at Albany, Albany, N.Y. USA.

The eye of Aplysia, the sea hare, is composed of thousands of small retinal and support cells. Recording from the optic nerve of the isolated eye shows that the activity is in the form of compound action potentials (CAP). These CAP are recorded in response to step increases in light intensity as an "on" response. These CAP are also recorded in constant light or darkness. Under constant conditions the CAP frequency and amplitude fluctuate in a circadian manner. The rhythm can be phase controlled by light-dark cycles and is relatively temperature insensitive. In constant darkness the CAP frequency shows a sharp increase at the projected dawn and then declines to a minimum during the projected dark. The rhythm has a free running period of about 27 hours. The amplitude of the CAP increases 2 fold during the sharp increase in frequency. The amplitude increase is due to recruitment of members of the retinal population. This can be demonstrated by anti-dromic activation of the optic nerve which shows a voltage dependent amplitude of the CAP. The synchrony of the population is brought about by synaptic coupling among the members. After exposure to constant conditions for several days the daily frequency profile approaches a symetrical distribution. Entrainment to an LD cycle shifts the peak of the profile toward the DL transition and produces a steep onset of frequency so that the profile resembles a sawtooth. The eye may be treated as a homogeneous population of coupled oscillators. (Supported by NIH grant NS 08443)

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DYNAMIC CHANGES IN ANTRAL VENOUS GASTRIN CONCENTRATION. B.M. Jackson, D.D. Reeder and J. C. Thompson. Dept. of Surgery, Univ. of Texas Medical Branch, Galveston, Texas.

Measurements of changes in the concentration of gastrin in antral venous blood during antral stimulation and suppression have not been reported previously. Methods: 18 anesthetized mongrel dogs were used. The venous drainage of the antrum was dissected to allow intermittent sampling of the total venous outflow which, when not diverted for sampling, flowed normally into the portal vein. The stomach was divided into antral and fundic pouches. Gastrin levels were measured by radioimmunoassay in samples of antral venous blood obtained during irrigation of the antral pouch with acetylcholine (Ach), 0.1 NHCI, saline or acidified Ach. Results: Antral stimulation with Ach produced a 430% ↑ (198 to 1067 pg/ml) in gastrin concentration within 2 minutes. Fundic acid output rose from 0,03 to 2,31 mEq/30 minutes. Gastrin levels remained significantly elevated for 8 hours following an initial 30 minute period of Ach irrigation. Antral irrigation with HCl promptly reduced both gastrin concentration and fundic acid output to basal levels. When utilized as the initial irrigant, acidified Ach produced a 350% ↑ in gastrin concentration (139 to 634 pg/ml) at 30 minutes. Conclusions: Stimulation of the isolated dog antrum produced an immediate elevation of measured gastrin concentrations in antral venous blood; there was a concomitant increase in fundic acid secretion. Acidification of Ach significantly diminished but did not abolish the release of gastrin. Brief antral stimulation causes prolonged release of gastrin if the antrum is shielded from acid secretion. Supported by grants from the John A. Hartford Foundation, Inc. and the U.S. Public Health Service.

RESPIRATORY RESPONSE TO INSPIRED CO₂ OF TURTLES EQUILIERATED AT DIFFERENT TEMPERATURES. Dept. of Physiology, Univ. of Pennsylvania, Philadelphia,

Pennsylvania, U.S.A.

In homeothermic vertebrates the respiratory minute volume ($V_{\rm E}$) tears a nearly constant relationship to the oxygen consumption ($V_{\rm O2}$), thereby stabilizing arterial PCO2 and pH despite changes in $V_{\rm O2}$. In many poikilothermic vertebrates, however, PaCO2 and pH vary with temperature and I have recently shown (<u>Physiologist</u> 13:230, 1970) that in the freshwater turtle, <u>Pseudemys scripta elegans</u>, the ratio, $V_{\rm E}/V_{\rm O2}$, varies inversely with temperature in a manner consistent with the acid-base changes. I now report the respiratory response to inspired CO2 (2, 4, and 6% CO2 in air) of this turtle equilibrated for at least three days at different temperatures (10, 20 and 30 C). The turtles, in contrast to many diving animals, responded strongly to CO2; at each temperature $V_{\rm E}/V_{\rm O2}$ increased steadily with increased CO2 until at 6% CO2 there was about a tenfold increase over the ratio during air-treathing. The relative response to CO2 was similar at each temperature so that the slope of the inverse relationship between $V_{\rm E}/V_{\rm O2}$ and temperature was similar for each breathing mixture. $V_{\rm E}$ increased with CO2 breathing but was relatively independent of temperature. (Supported by USPHS Grant No. HE 13845.)

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814 CATECHOLAMINE ANTAGONISM OF EXOGENOUS AND ENDOGENOUS ACETYLCHOLINE IN THE MAMMALIAN VENTRICULAR MYOCARDIUM. R. JACOB, H.F.KIENZLE, G.SIEBER, E. WILLE. Division of Cardiovascular Research, Physiological Institute, Tuebingen, Germany.

The mammalian ventricular myocardium is much less sensitive to acetylcholine (ACh) than the auricle. However, catecholamine antagonistic effects of ACh can be demonstrated in the ventricular myocardium. In the isolated cat papillary muscle a reproducible decrease of the contraction amplitude is caused by exogenous ACh (10-5 to 10-9 g/ml) if contractility has been increased by field stimulation. This negative inotropic effect of ACh cannot be exclusively explained by an inhibition of the catecholamine release emphasized by LÖFFELHOLZ and MUSCHOLL on the basis of rabbit heart experiments. Dose -response curves measured on the reserpinized muscle suggest an inhibition of the effects of exogenous noradrenaline and isoprenaline by exogenous ACh (10-6 g/ml). Furthermore a cholinergic substance (probably ACh) released by field stimulation inhibits the positive inotropic effects of exogenous catecholamines in the reserpinized or guanethidine-treated papillary muscle.

STUDIES ON THE POSITIVE CHRONOTROPIC EFFECTS OF STIMULATION OF THE VAGUS AND CERVICAL SYMPATHETIC NERVE TRUNK (CST) IN THE DOG. D. Jacobowitz and M. Singer. Dept. of Pharmacology, Sch. of Med., Univ. of Pennsylvania, Phila., Pa. USA.

Physiological and histochemical studies were made to investigate the vagal-induced cardioacceleration following atropine administration. Histochemical studies showed adrenergic axons which descend in the CST. Stimulation of the CST generally results in a positive chronotropic effect which is usually more pronounced with stimulation of the right CST than the left. This response appears to be mediated by catecholamines. It was found that the vago-sympathetic trunk deep in the neck divides into the CST and a segment of "pure" vagus. Stimulation of the "pure" vagus nerve usually produced a cardioacceleration after treatment with atropine. Histochemical studies showed that this effect was not mediated by adrenergic nerves within the vagus. The few adrenergic nerves in the "pure" vagus were associated with blood vessels. Superior cervical ganglionectomy caused a complete disappearance of these adrenergic nerves; the chronotropic response could still be elicited by stimulation of the vagus. The vagal "reversal" effect was mediated by catecholamines and was blocked by ganglionic blocking agents. The drug P-286 which has been shown to selectively block catecholamine release from the adrenal medulla, abolished the positive chronotropic response. It is suggested that this response may be at least partially mediated by a vagal innervation of cardiac chromaffin cells and that catecholamine released from the chromaffin cells acts both on the nodal tissue as well as on the cholinergic ganglion cells.

NEUROMUSCULAR ACTIVITY IN MAN: SAMPLING IN 30-MIN. TEST PERIODS WITH INTEGRATING NEURO-VOLTMETER AND DIGITAL COMPUTER. Edmund Jacobson and Richard E. Lange, Lab. for Clin. Physiology, Chicago.

Action-potential recording permits sampling determinations of neuromuscular contraction in selected muscle-groups with microvoltage integration at desired intervals ranging from 120 sec. to 110 m. sec. We have recorded from 4 to 6 channels while the subject sits or lies under repeatable controlled conditions. Surface electrodes are used where applicable. Information secured includes the following particulars: Although requested to remain at rest, most unselected subjects fail to relax to levels in neighborhood of zero microvoltage in any region. Generally muscles of legs or arms become more relaxed than muscles in head regions. Conspicuously active as a rule are eye-region muscles; also speech region muscles. All regions increase if the subject becomes excited. Applying the digital computer, data can be stored for statistical processing, including averaging, mean and standard deviation for individuals and/or for groups. Individuals are found to differ in the sites of their highest microvoltages during the test periods, but their curves are by no means characteristic like their thumbprints. Apparently there is difference in the same individual from time to time, as in "performance tests". Slides of tables illustrate the findings.

INHIBITION OF PANCREATIC SECRETION OF BICARBONATE BY NICOTINE. <u>Jacobson</u>, E. D., Konturek, S. J., Dale, J. and Johnson, L. R. Department of Physiology and Biophysics, University of Oklahoma Medical Center, Oklahoma City, Oklahoma, U.S.A.

The mechanistic link between eigarette smoking and duodenal ulcer formation is unknown. We investigated the effect of nicotine on gastrointestinal secretory processes responsible for formation and neutralization of acid in the duodenum. Conscious dogs were provided with one or more of the following preparations for chronic study: Heidenhain pouch (HP), gastric fistula (GF), pancreatic fistula (PF) and duodenal fistula (DF). Standard methods were used to measure: gastric juice volume, concentration of hydrogen and sodium ions; gastric mucosal blood flow; pancreatic juice volume, bicarbonate concentration and output. Nicotine had no effect on gastric secretion, the gastric barrier to H+ or Na+ or gastric mucosal blood flow. Effects of nicotine on the pancreas were:

MEASUREMENT PREPARATION STIMULUS ROUTE OF NICOTINE RESULT

MEASUREMENT PREPARATION STIMULUS ROUTE OF NICOTINE RESULT
Pancreatic bicarbonate PF,DF Secretin I.V. I.V. Inhibition
Secretin I.V. topical No effect
Endog. Secretin I.V. Inhibition
Endog. Secretin topical Inhibition
Inhibition of pancreatic bicarbonate secretion is dose-dependent, occurs soon after ad-

Inhibition of pancreatic bicarbonate secretion is dose-dependent, occurs soon after administering the nicotine and seems to be a competitive form of inhibition. Nicotine appears to act on both the duodenal mucosa to interfere with release of secretin and on the pancreatic secretory apparatus.

HEAT AND MECHANICAL VENTILATORY ENERGY LOST IN HYPERBARIC CONDITIONS. - Ch. Jacquemin, P.VARENE Laboratoire de Physiologie - C.H.U. 94. CRETEIL et C.E.V. (91) - Brétigny-sur-Orge. France.

The airways mechanical system is a double energy exchanger. 1. - The most part of work of breathing is dissiped against viscous gaseous resistance. 2. - The tracheobronchial tree regulated the physical characteristics of alveolar gases (temperature and humidity) by a countercurrent mechanism. In normaly ambient conditions lost of power (rate of energy) is small: 1 milliwatt per Kg of body weight for gaseous flow and one percent of basal metabolism for convective heat transfer. In hyperbaric environnement the increasing gaseous density modifies differently these two parts. 1. - At rest, power dissipated against airways resistances measured by plethysmographic technic increases as a function \sqrt{p} (p = gas density). During muscular exercice the pulmonary work of breathing is a direct function of power two of efficient ventila tory flow V measured in BTPS conditions $(V^{-}_{-})^{T}, V^{'}_{-}$ dt) and an exponential function of work load, whatever the ambient pressure is. In air diving (and equivalent density for Helium-oxygene mixture) the reduction of maximal voluntary work of breathing is not a limiting factor. 2. Theoriticaly, heat convective lost is a function of molar ventilatory flow (S.T.P.D. conditions) that is to say directly function of ρ . The measurements of mean expiratory temperature during hypercapnic hyperventilation drive (up to 5 liters per second) allow to compute the heat loss knowing the specific conductivity of gas. An empirical equation shows that thermic limit may be dependent of convectif heat lost through airways (45 per cent of 02 basal concumption at 20 acta in Helium at 0°C).

RESPIRATORY MECHANISMS INVOLVED IN THE PRODUCTION OF CONSONANTS AND VOWELS. Marc J. Jaeger, Dept. of Physiology, College of Medicine and Dentistry, Univ. of Florida, USA, and Institut de Physiologie, Universite de Fribourg, Suisse.

Sound intensity and pitch were recorded simultaneously with pressure drop and flow rate in the upper airways in five subjects during the phonation of consonants (s,f,sh,th) and of vowels (a,e,i,o,u). The area of the orifice where a sound originated (lips, teeth, or larynx) was estimated from the pressure vs flow relationship. The sound intensity of a given consonant is varied by adjusting both the pressure generated by the respiratory muscles and the orifice set by the oral muscles, i.e., the same sound level may be generated by a number of combinations of pressure drop and orifice size, the subject not being aware that he produces the same sound at the same sound level in different ways. The pitch of vowels is uniquely dependent on laryngeal factors while sound level is mostly regulated by varying the pressure. When a subject breathes a gas mixture other than air (80% He or SF₆) the sound level of vowels is most closely related to gas flow rate.

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NEURONAL ANALOGS OF CLASSICAL CONDITIONING IN APLYSIA CALIFORNICA.

Behrus Jahan-Parwar. Dept. of Biology, Clark University, Worcester, Mass. 01610 U.S.A.

Several neurons in the left pleural ganglion of <u>Aplysia californica</u> receive excitatory inputs following electrical as well as physiological stimulation of the visual and chemosensory pathways. Upon paired stimulation of these pathways in a type I conditioning paradigm some of the examined cells undergo a relatively long-lasting facilitation which in a few cases appear to be specific to the pairing of the applied stimuli. Since we also have evidence that intact <u>Aplysia californica</u> can be classically conditioned by using the same sensory pathways for conditioned and unconditioned stimuli, an analogy between the observed intracellular response plasticity in the examined cells of the left pleural ganglion and the behavioral conditioned response is demonstrated. (Supported by the NINDS grant #NSO8868-02 from the U.S.P.H.S.).

821 MICROPUNCTURE OF THE COLLECTING TUBULE IN RATS WITH HEREDITARY DIABETES INSI-PIDUS. Rex L. Jamison, John Buerkert, and Frank Lacy, Washington University Sch. of Med., St. Louis, Missouri, USA.

Water diuresis (WD) and antidiuresis (AD) were induced in rats with hereditary diabetes insipidus (Brattleboro strain) (mean wt. 65g), to study collecting duct function. In 18 rats, urine flow from the right kidney decreased from 19.5 \pm 1.38 SE to 1.81 \pm 0.16 μ /min; U/P osmolality (osm) increased from 0.51 \pm 0.02 to 4.11 \pm 0.24; and GFR decreased from 327 \pm 24 to 274 \pm 24 μ /min (P < .001 for all changes), while blood pressure remained unchanged. Micropuncture of the exposed papilla of the left kidney in WD revealed, TF/P osm of fluid from the collecting duct 1 mm proximal to the papillary tip (CDprox), 0.63 \pm 0.027, was greater than that from the collecting duct tip (CDtip), 0.55 \pm 0.024 (P < .001), while in AD, CDprox TF/P osm, 2.20 \pm 0.09, was less than CDtip TF/P osm, 2.71 \pm 0.11 (P < .001), suggesting that the processes of urinary dilution and concentration can both occur in the terminal collecting duct. The fraction of filtered water reabsorbed by the exposed collecting duct was 1.58 % \pm 0.32 in WD and 0.58 % \pm 0.08 in AD. The mean difference, 1.01 % \pm 0.29, was highly significant (P < .005). These findings imply that the volume of water reabsorbed by the terminal collecting duct in hydropenia is actually less than it is in water diures is .

INTRACELLULAR Ca-OVERLOAD AS THE DETERMINANT FACTOR IN THE PRODUCTION OF NON-CORONAROGENIC MYOCARDIAL FIBRE NECROSIS. J.Janke and A.Fleckenstein.

Physiological Institute, University of Freiburg, Germany.

Previous work (1,2) with 45Ca has shown that a number of non-coronarogenic cardiomyopathies result from an overload with intracellular Ca. This applies particularly to cardiac lesions caused by large doses of sympathomimetic amines, especially isoproterenol, since stimulation of adrenergic β-receptors increases the transmembrane Ca influx enormously. This, in turn produces (a) excessive activation of Ca-dependent intracellular ATP-ases and (b) swelling and functional deterioration of mitochondria, so that a massive deficiency of the cardiac high-energy phosphates occurs leading to structural damage as in anoxia or ischaemia. Factors which sensitize the myocardium to catecholamine-induced necrotization (corticosteroids, dihydrotachysterol, NaH₂PO₄) act by potentiation of intracellular Ca uptake; conversely hearts can be protected against these deleterious effects by suitable doses of Ca-antagonistic substances (KCl; MgCl₂; organic Ca-antagonists such as verapamil, D 600 or prenylamine) which greatly reduce the transmembrane Ca influx.

1) Fleckenstein, A.: Myokardstoffwechsel u. Nekrose in "Herzinfarkt u. Schock" ed. by L. Heilmeyer a. H. J. Holtmeyer, G. Thieme, Stuttgart pp. 94-109 (1968)
2) Janke, J., A. Fleckenstein a. W. Jaedicke: Pflügers Arch.ges. Physiol. 316, R 10 (1970); 319, R 9 (1970); 319, R 8 (1970)

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THE DISTRIBUTION OF AXONAL BRANCHES OF IA INHIBITORY INTERNEURONES IN MOTOR NUCLEI. E. Jankowska and W. Roberts. Dept. of Physiology, Univ. of Göteborg, Sweden.

Previous experiments have shown that interneurones monosynaptically excited from group Ia afferents and located in the ventral horn mediate reciprocal Ia inhibition of motoneurones (Hultborn, Jankowska and Lindström, J. Physiol. 1971, in press). Since posterior biceps and semitendinosus (knee flexor) motoneurones are inhibited from quadriceps (knee extensor), stimulation in the posterior biceps and semitendinosus motor nuclei would be expected to result in the antidromic activation of interneurones excited from quadriceps. Such an activation has been demonstrated by recording from single quadriceps interneurones in the ventral horn in L5-L6. It was found that their axons project caudally in the ventro-medial or lateral funiculi and branch extensively within the posterior biceps and semitendinosus motor nuclei in L7-S1. Single interneurones can be activated from a number of separate loci when using stimulus pulses of 2 μA or less through a second microelectrode. The conduction time along the axons and their branches was between 0.2 and 0.8 msec indicating a high conduction velocity for the axons.

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NON-MAST CELL HEPARIN. L.B. Jaques

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It is widely assumed that heparin occurs only in mast-cells. With the microelectrophoresis method for estimation of heparin (Jaques, Ballieux, Dietrich and Kavanagh, Can. J. Physiol. Pharmacol. 46, 351, 1967) applied to tissues digested with pronase, it is possible to determine heparin in 1 g samples of tissue with parallel histological examination of the tissue sample and further identification of heparin with enzymes of Flavobacterium heparinum. In rat lung, subcutaneous tissue, muscle and heart, the heparin/ mast cell ratio was 58, 47, 35, 49 pg/mast cell agreeing with values reported for isolated rat peritoneal mast cells of 22 and 44 pg/mast cell and values of 44 and 53 for lung and intestine reported by Marx based on anticoagulant assay. Values found for skin, stomach, large intestine, ileum were 67, 72, 133, 356 and by Marx for spleen and kidney, 165 and 440 pg/mast cell. These results indicate large amounts of heparin in these latter tissues not associated with mast cells. In dogs, there is a correlation between heparin and mast cells in livers of different animals to give a value of 5 pg/mast cell(corresponding to the smaller mast cells in this species). This accounts for only 1/4 to 2/3 of the heparin present in the liver. Values for dog intestine and dog lung are 14 and 36 pg/mast cell. There is considerable heparin in tissues other than that in mast-cells.

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MEMBRANE POTENTIAL CHANGES OF SPINAL MOTONEURONS EVOKED BY HIGH FREQUENCY EPICORTICAL STIMULATION IN RATS. R.W.Janzen, E.-J.Speckmann, H.Caspers. Inst. of Physiology, Univ., Münster (Westf.), German Fed.Rep.

In rats a series of cortical seizure discharges is usually associated with a sustained depolarization of lumbar motoneurons (LMN). The mechanisms of this effect were studied in greater detail by electrical stimulation of the cerebral cortex with various pulse frequencies: l) Single electrical stimulation of the cerebral cortex evoke on LMN a sequence of EPSPs composed of oligo- and polysynaptic components. With increasing stimulation frequency the seperated postsynaptic potentials fuse into a sustained depolarization, the time course of which may show either an early or a late peak. 2) Plotting the integrated depolarization shifts against pulse frequencies reveals a nonlinear relation in the range of 10-100 p/s. A particular dip of the curve is found with 50/s stimulations. 3) Cortically induced depolarizations of LMN may exceed a critical level at which spike generation fails. The findings can be attributed to special recruiting mechanisms in supraspinal structures. They resemble those observed in certain seizure states.

826 ASSOCIATION AND PRIMARY RESPONSES IN THE FORMATION OF TEMPORARY CONNECTIONS IN THE CAT. T.D.Javrishvili. Inst. of Physiology, Georgian Academy of Sciences, Tbilisi, USSR.

Evoked responses (ER) to clicks from association (g. suprasylvius), auditory and visual cortex in the freely moving cats with implanted electrodes were studied. Amplitude changes of the association and primary responses (AR and PR) to "indifferent" acoustic stimuli, during habituation, distraction, conditioning and acute extinction were compared. The results are as follows: (I) the amplitude of the ARs (and of the PRs in a lesser degree) depends rather upon the biological meaning of the stimulus than on its physical strength; (2) the habituation to the indifferent rhythmic acoustic stimulation develops, being far more pronounced in the association cortex; (3) with the formation of temporary connections the ARs arise, which, compared to the PRs, considerably increase in amplitude, especially in their negative phase. The ARs diminish after strengthening of conditioned reflex, increasing again during the acute extinction; (4) we conclude that the determination of the novelty and meaning of sensory information is more acutely and distinctly reflected in the association cortex than in the primary sensory one.

ACTIVITE DES NEURONES DEGLUTITEURS BULBAIRES. A. Jean et C. Roman. Lab. Neurophysiologie générale, Faculté des Sciences St-Jérôme, Marseille, France

L'activité des neurones déglutiteurs bulbaires a été étudiée chez des moutons décérébellés, faiblement anesthésiés au fluothane, à l'aide de microélectrodes de tungstène. La zone explorée correspond à la réticulée sousjacente au faisceau solitaire. Les activités unitaires recueillies lors de la déglutition peuvent être classées en 2 catégories : des activités précoces se produisant avant et pendant le stade bucco-pharyngé ; des activités tardives contemporaines du stade oesophagien. Différents critères nous permettent d'affirmer que les générateurs enregistrés ne correspondent ni à des motoneurones ni à des afférences déglutitrices. Il s'agit d'interneurones faisant partie du "centre" qui organise la séquence de contractions caractéristiques de la déglutition. Lors de la stimulation des afférences déglutitrices, certaines cellules présentent une première activation (1 à 2 potentiels) de latence souvent très faible (2 ms), suivie d'une seconde décharge plus tardive lorsque l'animal déglutit. Ces cellules sont vraisemblablement des neurones de relais de premier ou second ordre situés dans le noyau du faisceau solitaire comme le confirment les contrôles histologiques. Ainsi le noyau du faisceau solitaire ne constituerait pas une simple station pour les influx afférents : il existerait déià entre ses cellules tout un système d'interconnexions responsable de l'organisation d'un mouvement.

828 MEASUREMENT BY DIRECT CALORIMETRY OF BODY THERMAL INSULATION IN OBESE AND LEAN SUBJECTS. E. Jéquier, B. Ruedi, P. Magnenat and A. Vannotti. Dept. of clinical Physiology and Medicine, University of Lausanne, Switzerland.

Calculation of body thermal insulation (I_b) requires the precise measurements of heat flow through the skin and the determination of the temperature gradient between internal and mean skin temperatures. In this study, measurements of heat losses were obtained by direct calorimetry in 32 obese and in 26 control subjects. At low ambient temperature ($T_a = 20^{\circ}\text{C}$), the skin blood flow is insignificant and I_b only depends on the physical properties of the tissues: in this condition, I_b was found to be significantly larger in the obese than in the control subjects; furthermore, I_b was roughly proportional to the degree of obesity. It is of interest that I_b of the obese women was larger than I_b of the fat men (for a similar degree of obesity). In a neutral thermal environment ($T_a = 30^{\circ}\text{C}$), the value of I_b is decreased by the skin blood flow; however, I_b of the obese subjects was also found to be greater than I_b of the controls. These results support the concept that the increased I_b of the obese subjects contribute to conserve energy, especially when they are exposed to cold.

(this work was supported by the Nestlé Foundation).

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THE INFLUENCE OF EPINEPHRINE, CORTISOL, ALDOSTERONE AND ESTROGENS ON THE RESISTANCE OF THE CENTRAL NERVOUS SYSTEM TO ISCHEMIA DURING ONTO-GENY OF THE RAT. L.Jílek, S.Trojan. Inst.of Physiology, Med.Faculty, Charles Univ., Prague, CSSR.

Ischemia of the central nervous system was brought about by positive radial acceleration of 10g. The measure of resistance was irreversible arrest of respiration. Epinephrine (20 gamma/100 g; s.c.) increased resistance in 5-day-old rats and in adult animals. Cortisol (10 mg/100 g; i.p.) had a favourable effect from birth till day 25, aldosterone (10 mg/100 g; i.p.) till day 5 of the rat. Estrogens (oestradiolum dipropionicum, stilboestrolum diphosphoricum - 500 gamma/100 g; i.p.) augmented the resistance in rats during the whole of ontogeny; the greatest effect being at the weaning time (25-day-old rats). The results indicated that in the immature nervous tissue the hormons have a direct effect on the metabolism in the brain. In adulthood the effect is mediated by systemic functional and metabolic changes.

AUTOREGULATION AND REACTIVE HYPEREMIA IN SKELETAL MUSCLE CAPILLARIES. Paul C. Johnson and Kenneth S. Burton. Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724, U.S.A.

Reduction of arterial pressure to isolated skeletal muscle produces an initial fall in flow followed by a partial return to control levels. Reactive hyperemia after complete arterial occlusion is typified by a rapid rise to high flows followed by an exponential decay to control levels. The time course of both phenomena has been interpreted as evidence for metabolic control of resting blood flow in skeletal muscle. We have used a dual slit photomultiplier tube technique to measure red cell velocity and flux in single capillaries of cat sartorius muscle during these two procedures. Reduction of arterial pressure produces a sustained fall in red cell velocity in many capillaries. However, a definite autoregulatory response is evident in some capillaries with red cell flow exceeding the control level during hypotension. In reactive hyperemia, flow in many capillaries rises to an early peak then falls precipitously and may stop for 10 to 30 seconds. In some capillaries there is a slower rise in flow and a more gradual return. It appears that the time course of gross flow adjustment does not reflect the behavior at the capillary level. Moreover, capillary flow patterns are not readily explicable in terms of metabolic mechanisms and a component of myogenic activity may be involved in autoregulation and in reactive hyperemia. (Supported by AHA grant-in-aid and NIH grant AM 12065).

EYE MOVEMENTS AND EFFERENCE COPY. J.R. Johnstone and R.F. Mark. Department of Physiology, Monash University, Clayton, 3168, Australia.

During voluntary eye movements there is stimulation of the retina which however does not lead to any sensation of visual movement. Helmholtz suggested the reason for this was the "sense of effort" which accompanies such movements and enables a proper interpretation to be made of the corresponding visual input. In recent years this theory has been restated in terms of neural circuits: efference to the eye muscles is accompanied by a collateral discharge, efference copy, to the visual centres of the brain. However, not all eye movements should be accompanied by efference copy. Some are produced specifically to maintain a constant visual field. In particular, the slow phase of nystagmus and counter rotation are both produced by head movements and both maintain fixation. We have been able to record neural activity from the tectal commissure of goldfish which appears to have all the required properties of efference copy. These neurons fire during the regular saccadic movements produced by a restrained goldfish and they encode time, direction and amplitude of the movement. They also discharge during the fast phase of vestibular nystagmus produced by rotation about the vertical axis but they are silent during the slow phase and also during counter-rotation.

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ROLE OF CALCIUM IN THE CONTROL OF POTASSIUM ACCUMULATION BY SMOOTH MUSCLE.

A. W. Jones, J. Gulati and M. L. Swain. Bockus Res. Inst. and Physiol. Dept., University of Pennsylvania, Philadelphia, Pennsylvania, U.S.A.

Whereas the controlling action of Ca has often been studied on the electrical and mechanical behavior of smooth muscle, little is known concerning the interaction of Ca with ion accumulation processes. The accumulation of K by intestinal, uterine and vascular smooth muscles can be quantitatively described, for a wide range of [K]_o, by a model which takes into account the interaction of ions with a limited number of fixed sites. When [Ca]_o is systematically decreased there is a decrease in the selectivity (K_{K} , N_{A}) exhibited by the accumulation process for K over Na. The maximum decrease, accomplished in a Ca-free solution, was greater in canine carotid artery than the taenia-coli of the guinea pig. The "dose-response" relation between [Ca]_o and K_{K} , N_{A} indicated half of the maximum shift occurred at [Ca]_o of about 0.1 mM for both smooth muscles studied. It is suggested that the effect of [Ca]_o on K_{K} , K_{A} reflects the uptake of Ca onto a small number of controlling sites, and that half saturation of these sites occurs at [Ca]_o of about 0.1 mM.

(Supported in part by USPHS HE 07762 and N ONR 551 (54).)

EVIDENCE IN FAVOUR OF A FAST FEEDBACK CONTROL OF ACTH SECRETION BY CORTICOSTERONE.

M.T. Jones. Sherrington School of Physiology, St. Thomas's Hospital Medical School London, S.E.1.

Vehicle or corticosterone was infused i.p. in male rats weighing 150-200 g at a rate of 10 ug/min for 10 min. The corticosterone infusion caused a rise in plasma steroid level which reached a peak of 55.2 + 3.7 ug at 10 min. Stress of bilateral sham adrenalectomy applied to vehicle-infused rats at 2, 5 or 10 min. after beginning of the 10 min infusion showed a corticosterone stress response of 20 ug/100 ml. Corticosterone-infused rats at these times showed a marked suppression of the stress response. However, by 20 min.(i.e. 10 min. after end of infusion) the stress response in the corticoid-infused rats had returned to normal even though the blood corticosterone level was still high at the time of stress.

It is concluded that physiological doses of corticosterone can rapidly inhibit the corticotrophic response to stress and that this inhibition occurs only during the early period following corticoid administration.

834 SYNCHRONIZATION OF CARDIAC PACEMAKER CELLS. H.J.Jongsma and C.C.Hollander. Dept. of Physiology, Univ. of Amsterdam, The Netherlands.

We have tried to verify our hypothesis that pacemaker cells have a synchronizing action upon each other. For that purpose, the contraction frequency of cultured rat heart cells was measured during the time, in which the originally isolated cells form a monolayer of interconnected cells. From 20 hours until 45 hours after plating the cells, 1000 contraction intervals were measured every hour. Mean value and standard deviation (SD) of these intervals were calculated and plotted against time elapsed since plating. The results show that frequency increases steadily during growth, reaching a plateau of 2.3 Hz after 45 hours, while the SD decreases from 50% at 22 hours to 2.5% at 35 hours. Thus, isolated cells beat very irregularly. Regularity increases concomitantly with the increase in number of interconnected cells. To explain these results we propose that pacemaker cells synchronize during diastole by electrotonic interaction between interconnected cells and that a certain number of cells is necessary to obtain regularity. Electrophysiological evidence for this proposal is provided by the following facts: 1. There is extensive electrotonus between heart cells in monolayers (space constant of 0.4 mm, assuming the monolayer to be a thin plane sheet). 2. Intracellularly applied current changes the frequency of such monolayers.

THE FILTERABILITY OF INULIN AND POLYETHYLENE GLYCOL THROUGH THE GLOMERULI OF RABBIT KIDNEY. K.E.Jørgensen, J.V.Møller, and M.I.Sheikh. Inst. of Med. Biochemistry, Univ. of Aarhus, 8000 Aarhus C, Denmark.

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It has been reported by Berglund on the basis of comparisons of the clearance of inulin and low MW preparations of polyethylene glycol that inulin is only partially filterable through the glomerular membrane of the rat kidney. In the present study we have compared the renal excretion (in the rabbit) of inulin'(MW:5000) and of different MW preparations of polyethylene glycol (PEG). It was found that the clearance of PEG-1500 and -4000 was identical with that of inulin; in contrast the ratio between PEG-6000 and inulin clearance was 0.89 ± 0.03 (S.D.). Chromatographic experiments on Sephadex columns established that the elution pattern of inulin from urine samples was identical with that from plasma samples. Furthermore, PEG-4000 and -6000 appeared in advance of inulin. Ultrafiltration through cellophane membranes gave the following filterability results: Inulin: 43 %, PEG-1500: 45 %, PEG-4000: 7 %, and PEG-6000: 0.4 %. It is concluded that, in contrast to PEG-6000, inulin, PEG-1500, and -4000 are completely filterable through the pores of the glomerular membranes. This is in keeping with the gel filtration and ultrafiltration experiments which show that the preparations of PEG have a more expanded structure than that of inulin.

AXIAL MASS DISPLACEMENT BY VENTILATION IN MAN. W.T. Josenhans and C.S. Wang. Dept. of Physiology, Dalhousie University, Halifax, N.S., Canada.

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Since contraction of the inspiratory rib-cage muscles displaces body tissue mainly in a direction perpendicular to the body's longitudinal axis, a footward axial mass displacement reflects mainly diaphragmatic shortening alone. Therefore, partitioning of the tidal volume into a rib cage and an abdominal component becomes possible in supine position by means of an ultralow-frequency ballistograph. We investigated the contribution of the main inspiratory muscles to ventilation in man and found 1) during normal breathing the mean diaphragmatic contribution to inspiration amounts to 67% in healthy men and to 60% in women. 2) The diaphragmatic contribution to inspiration increases during growth from a mean of 50% at 12 years of age to level off to adult values between 20 and 25 years. 3) Enlarging external dead space, leading to a three-fold increase in ventilation, caused a 30% increase in volume moved by diaphragmatic action, whereas the rib-cage contribution increased 270%. An increase in diaphragmatic contribution to inspiration was found in singers and wind-instrument players, in obesity, paraplegia, emphysema, and restriction of the rib cage (ankylosing spondylitis); a decrease in asthma, emphysema, hemidiaphragm, and muscular dystrophy. Not much change was seen in pregnancy. In some cases with ankylosing spondylitis and paraplegia a diaphragmatic contribution of over 120% was seen, indicating that the diaphragmatic piston action would have inspired 120% of a tidal volume, had not the rib cage 'giver in'.
Supported by The Muscular Dystrophy Associat on of Canada.

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THE ROLE OF ADRENERGIC RECEPTORS IN THE REGULATION OF MYOCARDIAL TISSUE BLOOD FLOW.

A. Juhász-Nagy and M. Szentiványi, Clinic for Cardiovascular Surgery, University

Medical School, Budapest, Hungary.

Tissue blood flow in the left ventricle of pen chest dogs was registered with

the aid of the heat clearance technique. Coronary sinus outflow was measured simultaneuosly by means of a rotameter. Supramaximal stimulation of the stellate ganglion as well as intravenous or intracoronary administration of noradrenaline elicited a considerable increase both in the myocardial thermal clearance and in the sinus outflow. The degree of the coronary dilatation registered by the rotameter, however, was significantly greater than that of the augmentation in the tissue blood flow, When pure alpha adrenergic activity is unmasked by blockade with propranolol /0.3 -0.5 mg/kg/, the relation of these two effects gets reversed. After beta adrenergic blockade sympathetic excitation brought about coronary constriction. On the other hand, alpha adrenergic activation did not induce a comparable flow decrease in the myocardial tissue. Instead of declining, myocardial heat clearance often increased considerably. The latter effect was occasionally preceded by a short and insignificant'constriction', which coincided with the initial phase of the sinus outflow decrease. The results suggest that activation of the coronary constrictor fibres eventually creates favourable conditions for an improuved distribution of the coronary flow at the capillary level.

838 STUDIES ON THE EXOCRINE FUNCTION OF THE PANCREAS OF RATS AFTER CHRONIC CANNULATION. Agnes Juhász Nagy Zsinka. Inst. of Nutrition, Budapest, Hungary.

A new method has been elaborated for the separated collection of the pancreatic and duodenal juice and the bile of rats. Polyethylene cannulas were implanted into the proximal and distal portion of the common biliary duct for the collection of the bile and the pancreatic juice. Both cannulas were connected by means of a three-branched extracorporeal shunt with a similar polyethylene tube inserted into the duodenum. In unanaesthetized animals 8-10 days postoperative to the implantation the pancreatic juice has been studied for quantity, for total protein content and for trypsine, lipase and amylase activity, respectively. The results of the chronic cannulation experiment were compared with those obtained in narcotized animals using acute cannulation. The procedure proved to be a suitable technique for physiological investigations as well as for toxicological screenings.

839 EFFECT OF BETA-ADRENERGIC BLOCKADE ON PLASMA VOLUME IN MAN. S. Julius, A. Pascual. Univ. of Mich. Med. Ctr., Dept. of Int. Med., Hypertension Unit, Ann Arbor, Mich. USA

Twenty-seven young males (ages 18-26) were studied. Resting cardiac output (indocyanine green), plasma volume (Evans blue) and hematocrit were determined. Measurements were repeated 7 minutes of .2 mg/kg of propranolol i.v and after additional .04 mg/kg of atropine i.v. Changes of plasma volume were also calculated from changes of plasma protein and hematocrit. After propranolol, plasma volume decreased for average 12%, and remained decreased after atropine. Plasma volume remained low regardless whether cardiac output was low (after propranolol) or normal (after atropine). Similarily, plasma volume levels were not related to trends in the central venous pressure and peripheral vascular resistance. Changes of plasma volume calculated from hematocrit were less impressive (-5%) than from optical density and plasma proteins. These findings can best be explained by increased postcapillary venous tone resulting in enhanced capillary filtrations and red blood cell trapping. Apparently a resting dilatory postcapillary tone is removed by propranolol and alpha-adrenergic venoconstriction prevails.

ALTERATION OF INTESTINAL HEMODYNAMICS DURING THE DEVELOPMENT OF THE GASTROINTESTINAL RADIATION SYNDROME. J. Kabal and S. J. Baum. Armed Forces Radiobiology Research Institute, Defense Atomic Support Agency, Bethesda, Maryland.

The impairment of the small intestinal blood flow has been implicated in the deteriorating sequence of the Gastrointestinal Radiation Syndrome. However, the mechanism of this impairment has not been elucidated. The objective of this study was to measure the functional vascular integrity of the small intestine in relationship with its morphological alterations during the postirradiation period. Dogs were exposed to 1500 rads (midline tissue dose) of mixed gamma-neutron radiation. Hemodynamic parameters of an <u>in situ</u> intestinal loop were measured in response to the systemic administration of norepinephrine, isoproterenol and gradual bleeding-reinfusion. The results indicate that 48 hour postirradiation when the capillaries are still intact and the hemodynamic parameters are not altered yet, the functional integrity of the intestinal vasculature is already significantly changed. The intestinal resistance vessels of the irradiated animals did not exert "autoregulatory escape" as compared with the controls. After 72 hours the vasocompensation to the sudden blood pressure changes was markedly delayed. The fluctuation of the intestinal resistance values during the bleeding-reinfusion period demonstrated the presence of the postirradiation neurohumoral inbalance. Autoregulation was not observed during the postirradiation period. On the basis of these results it is postulated that the terminal cardiovascular collapse in irradiated animals is due to the development of "Intestinal Ischemic Shock."

NEURAL CENTERS REGULATING GASTRIC SECRETION*. M.Kadekaro, C.Timo-Iaria, L.P. Eira Velha, L.E.Ribeiro do Valle. Dept. Physiol.Pharmacol., Inst.Biomed.Sci. University of São Paulo, São Paulo, SP, Brazil.

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2-deoxy-d-glucose, 2-DG, was used as a tool to disclose neural centers regulating gastric secretion. Ninety cats with a permanent gastric cannula were tested with 2-DG, 60mg/kg, before and after central lesions were made.

1. Decerebration abolished secretion. 2. Destruction of large thalamic and hypothalamic areas 'failed to block the secretory response to 2-DG. 3. Lesion of the medial forebrain area (MFB) at the level of the median and posterior hypothalamus suppressed secretion. 4. Lesions involving the globus pallidus also almost suppressed secretion. 5. Destruction of the areas which contribute fibers to the MFB, such as septum, amygdala, preoptic area, and cortex, did not disturb the gastric response. It is suggested that intrafascicular neurons of the MFB sensitive to changes in blood glucose levels convey the input to the globus pallidus, from which the output of a gastrosecretory reflex emerges.

*Supported by the São Paulo State Research Foundation (FAPESP)

SODIUM AND POTASSIUM CONCENTRATIONS IN CAT SUBMAXILLARY GLAND SALIVA EVOKED BY SYMPATHETIC AND PARASYMPATHETIC NERVE STIMULATION. N. Kahn, Eda Cole, and I.D. Mandel. Dept. of Pharmacology and Divisions of Dental Hygiene and Stomatology, Columbia Univ., New York, N.Y., U.S.A.

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The effect of electrical stimulation of the parasympathetic nerve to the cat submaxillary gland on the relationships between flow rate, Na, and K content has been studied extensively. In the present study these relationships were studied in saliva evoked by sympathetic stimulation as well. In chloralose-urethane anesthetized cats, the peripheral cut ends of the autonomic nerves to the glands were stimulated every 70 sec with 30 sec trains of 1.0 msec pulses of 1.0 mamp intensity. At each stimulation frequency the first .15-.20 ml was discarded and the next .15-.20 collected and analyzed for Na and K. K concentration-flow rate relationships were similar with sympathetic and parasympathetic stimulation except that the sympathetic saliva had significantly higher levels of K at all comparable flow rates. At flow rates > .05 ml/min the difference ranged between 45-75 mg%. At rates < .05 ml/min K was usually inversely related to flow rate. At about .05 ml/min K levels plateaued and did not vary significantly at higher flow rates. Na levels in both types of saliva were directly related to flow rate. Na levels in sympathetic saliva were either greater than or equal to those in parasympathetic saliva secreted at a comparable flow rate. (USPHS Grants DE02685, NS34336 and HE12738).

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UPTAKE AND RELEASE OF CALCIUM FROM MAMMALIAN C FIBRES. \underline{P} . Kalix, Inst. of Pharmacology, Univ. of Geneva, Switzerland.

Desheathed rabbit vagus nerves were loaded with ⁴⁵Ca and uptake and efflux measured by liquid scintillation counting. The uptake of radiocalcium reached saturation after 2 hr: out of a total of 1.85mM intracellular Ca/kg wet nerve (Dubuis, Thesis, Geneva 1969) 46% could then be labelled. Addition of La or Pr decreased the rate of influx by about 50%. The rate constant for the Ca efflux decreased with time, two different phases of Ca efflux with time constants of 10.7 and 170 min could be distinguished. Lowering the temperature decreased the rate of Ca efflux of both phases with a Q_Q of 1.4. Addition of inhibitors of active transport (ouabain, ethacrynic acid) or metabolism (CN⁻, 2,4-DNP, IAA, p-CMB) had no effect on the Ca efflux. On the other hand replacement of extracellular Na by choline lowered the efflux by about 1/3, and the efflux increased upon addition of extracellular Na. Further, local anesthetics, tetrodotoxine, veratridine, bretylium and guanethidine did not influence the efflux. The results suggested that most of the exchangeable Ca in the vagus nerve is bound at intracellular binding sites of different affinities, and that the efflux is partly mediated through a Na/Ca exchange system different from the Na carrying system responsible for excitation.

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ACTIVITY OF BARORECEPTORS AND REGULATION OF THE ARTERIAL BLOOD PRESSURE IN EXPERIMENTAL HYPER- AND HYPOTENSION. W. Kalkoff,
A. Brattström. G. Brand, B. Kalkoff-Ganse. Inst. of Physiology,
Med. Academy Magdeburg, Germ. Dem. Rep.

Experiments were performed to study the input/output relationships of the vascular reflexes on anaesthetized dogs. Arterial blood pressure, carotid sinus pressure and impulse activity of the carotid sinus nerve (single and multifiber preparation non-sequential and sequential intervalhistograms) were measured. In different studies it was further shown by quantitativ analytical techniques with simultaneous counting of baroreceptor impulses from the non-dissected sinus nerve the stativ input/output relationships of the carotid sinus reflex after resetting of the arterial blood pressure elicited 1) by application of adrenaline topicaly on the carotid sinus area (reflex hypotension by excitation of the carotid sinus tonic depressoric C-fibers). 2) by GOLDBLATT-clamping (renal hypertension) and 3) by electrical stimulation of a spinal nerve (N. Femoralis). Results of the experiments will be discussed.

ADRENERGIC CONTROL OF OVULATION. <u>Ilva Kalnins and K.B. Ruf</u>, Inst. de Physiologie, Ecole de Médecine, <u>Univ. de Genève</u>, <u>Geneva</u>, <u>Switzerland</u>.

Central chemical sympathectomy was attempted in female rats with 4-day oestrous cycles by injecting 6-hydroxydopamine (6-OH-DA) into a lateral brain ventricle. A single injection of 250 μg during oestrus or dioestrus I (n=56) blocked the following ovulation in >80%. Injections during dioestrus II were less effective. The vehicle alone (n=10) and the i.v. injection of the 10-fold dose of 6-OH-DA did not interfere with ovulation. Nine out of 10 rats pretreated with 6-OH-DA during oestrus and injected with LH during the following "critical period" ovulated, thus indicating a central site of action of 6-OH-DA. Electrical stimulation of the basal hypothalamus of rats blocked with 6-OH-DA (n=13) caused ovulation in only 3 cases. Ovulation was not restored by intraventricular injection of dopamine (1.25 - 40 μg , n=10) during the following procestrus. The dose of 6-OH-DA used causes rapid disappearance of catecholamine fluorescence in periventricular areas such as the tubero-infundibular tract (J. Constantinidis et al., in press). The data show that central sympathectomy may block ovulation and thus provide new evidence for a role of amines in the central control of gonadotrophin release. (Supported by Swiss Natl. Fndn. for Scientific Research).

IN VIVO DEMONSTRATION OF LH-, FSH-RELEASING AND PROLACTIN-INHIBITING ACTIVITY IN HYPOPHYSI-AL PORTAL BLOOD OF MALE RATS AFTER INJECTION OF DOPAMINE INTO THE THIRD VENTRICLE. 1.A. 846 Kamberi, R.S. Mical & J.C. Porter. Univ. Tex. Southwestern Med. Sch., Dallas, Tex., USA. Pituitary stalk and femoral artery blood was collected from male rats injected with 1.25 µg dopamine hydrochloride (DA) via the third ventricle. FSH- and LH-releasing and prolactin (LtH)-inhibiting activity was determined by infusion of stalk or femoral plasma (2 µl/ min/30 min) into a hypophysial portal vessel (PV) of intact rats. Prior to infusion, the concentrations in peripheral plasma of LtH, LH, and FSH were 30.4 \pm 2.21 ng/ml (mean and SE), 3.6 \pm 0.35 ng/ml, and 0.50 \pm 0.36 μ g/ml, respectively. Infusion of femoral plasma had no effect on the concentrations of these hormones. When stalk plasma from donors given DA was infused into a PV, plasma levels of LH and FSH increased and LtH decreased. LH levels after 10, 20, and 30 min of infusion were 0.6-, 2.2-, and 2.9-fold greater than the preinfusion level, respectively. Corresponding FSH concentrations were 1.3-, 1.6-, and 2-fold greater than the preinfusion level. Infusion of stalk plasma from DA-treated donors caused a fall in LtH levels. LtH levels after 10, 20, and 30 min of infusion were 68, 42, and 31 percent of the preinfusion level, respectively. On cessation of infusion, LH and FSH concentrations in plasma began to fall and that of LtH to rise. Infusion of stalk plasma from saline-treated rats into a PV caused only slight increases in the plasma levels of LH and FSH and a decrease in the level of LtH. These results suggest that dopaminergic neurons may regulate the release of certain hypophysiotropic substances. (Supported by NIH Grant AM01237 and a grant from The Population Council, New York, N.Y.)

INFLUENCE OF ISOPROTERENOL (I), EPINEPHRINE (E) AND NOREPINEPHRINE (NE) ON HIGH ENERGY PHOSPHATE COMPOUNDS OF THE MYOCARDIUM AT VARIOUS EXTRACELLULAR PH VALUES. H.Kammermeier, V.Ziegler, W.Krautzberger and B.Kammermeier. Dept. Physiology, Medical Faculty, Technical University, Aachen, Germany

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High energy phosphates were determined in guinea pig myocardium (heart lung preparation) under constant work load of the heart at pH 7.0, 7.4 and 7.9, respectively. At pH 7.4 I,E and NE induced a decrease of these compounds, particularly of creatinephosphate (CP), the extent of which was similar to that observed during severe pressure load. Typical dose response relationships (DRR) were obtained. In equal concentrations I was found to be more effective than NE and E. The changes of CP were paralleled by changes of dp/dtmax and of heart rate. Under severe pressure load cate-cholamines did not cause a further decrease of CP. The DRR for changes in CP content were shifted to the left after elevating the extracellular pH up to 7.9 by reduction of pCO2, and shifted to the right after lowering the pH to 7.0 by increasing pCO2. The DRR for inotropic and chronotropic effects were not influenced characteristically. At high extracellular pH the extent of the catecholamine induced decrease of CP became markedly enhanced, though the inotropic response proved to be reduced. These results indicate that after changes of extracellular pH the functional and metabolic effects of catecholamines on the myocardium tend to dissociate.

MECHANISM OF ACTION OF ALTERED LOBAR BLOOD FLOW ON BRONCHOMOTOR TONE, J. P. Kampine, R. L. Coon, W. J. Stekiel and E. O. Henschel. Dept. of Physiology, Med. Col. of Wisconsin, Milwaukee, Wis. U.S.A.

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The effect of a graded reduction in nulmonary blood flow on bronchomotor tone was studied with a technique involving alternate use of the constant volume ventilation method (Gerst et al., J. Clin. Invest. 38:524, 1959) with the ventilation overflow method (Konzett and Rossler, Arch. Exptl. Pathol. Pharmakol. 195:71, 1940) in the in situ blood perfused left lower lobe of the canine lung. Graded reduction of lobar flow (465 -0 ml/min x 100 gm lung) was associated with an increase in airway resistance and a decrease in lung compliance, associated with a fall in alveolar $P_{\rm CO2}$. Fifty per cent of these changes in airway resistance and lung compliance occurred when flow was reduced from 65-0 ml/min x 100 gm lung. The effects of a graded reduction in alveolar $P_{\rm CO2}$ and perfusate $P_{\rm CO2}$ were studied during constant flow perfusion in a recirculating system. Decreased alveolar $P_{\rm CO2}$ resulted in an increase in total resistance with the greatest changes seen at an alveolar $P_{\rm CO2}$ below 20mm Hg. These changes were reversed by addition of CO2 to the inspired gas mixture or perfusate and by constant infusion of lactic acid at a rate sufficient to reduce the pH of the perfusate to 7.35 or below. Addition of sodium bicarbonate to the perfusate in the absence of CO2 produced an increase in airway resistance and a decrease in lung compliance associated with an increase in pH. It appears that the changes in airway resistance and lung compliance associated with reduced lobar blood flow are due to a reduction in $P_{\rm CO2}$ and an increase in pH.

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DYNAMIC CHANGE OF CELL COMMUNICATION IN SUBCUTANEOUS SOLID TUMOR (MH134-C3H/He). $\underline{Y.Kanno}$ and $\underline{Y.Matsui}$. Physiol. Dept. Hiroshima Univ. School of Dentistry, Hiroshima, Japan.

It is well known that there is intercellular communication between cells of wide varieties in normal epithelia. Cellular communication, however, is depressed by treatments that are generally known to suppress energy metabolism and are Ca-poor in environmental solution. In any cancer, extreme depression appears and transplantable ascites cancer cells (MH134-C3H/He) are completely isolated and have no communication at all. When isolated cancer cells are inoculated in subcutaneous space, solid tumor is established in about 1 week and the survival of the host mouse is considerably prolonged and hosts finally die as a result of metastasis. It is found that established solid tumor produced in mouse is divided into 3 parts. Viable part A, mostly nectrotic part N and a small viable part C which originates in N part and spreads to normal tissue of the host beneath the tumor. Part C is mostly responsible for the formation of metastasis in all most lymph nodes. Communication ratio is less than 0.0006 (limit of resolution of our electrophysiological technique) in ascites cells, 0.0044 in part A and 0.0012 in part C. There are some relationships between cancer malignancy and cell communication at least in survival and metastasis formation.

ARTERIAL PRESSURE DROP AT CHANGES OF THE VASCULAR RESISTANCE IN CEREBRAL AND HIND LIMB CIRCULATION. E. Kanzow, J. Jansen and D. Dieckhoff, Dept. of Physiology, II, Univ. of Goettingen, German Fed. Rep.

Pressure drop from aorta to cerebral and hind limb arteries was measured on chloralose-urethan anesthetized cats. In the middle cerebral artery and in a metatarsal artery of the hind limb the blood pressure was found to be reduced by 20 - 30 % and in pial arteries, 30 - 40 micron in outer diameter, by 40 % of the aortic pressure. This demonstrates that a remarkable part of vascular resistance is located in greater vessels. Therefore the effect of vascactive agents was studied. It was seen that these vessels contribute also to changes of the total flow resistance in a great extent.

851 VOLTAGE CLAMP EXPERIMENTS ON UTERINE SMOOTH MUSCLE. C.Y. Kao. Department of Pharmacology, State Univ of New York, Downstate Medical Center, Brooklyn, N.Y., U. S. A.

Isolated myometrial strips from 16-21 day pregnant rat uterus have been voltage-clamped in a double sucrose gap unit. Resting potential = -49.1 \pm 1.2 mV (n=82); spike = 48.2 \pm 0.7 mV (n=100). The voltage-current relation on hyperpolarization is linear. On depolarization, an early transient inward current (Ia) is followed by a late outward current (Ib). In the V-1 relation, Ia is N-shaped and has a (-) resistance region. After correcting for leakage current E_a = 18.6 \pm 1.4 mV (n=52). E_a shifts by an amount expected of a Na⁻-selective membrane when $\lceil \text{Na}^+ \rceil_0$ is reduced from 144 to 72 mM, but not when $\lceil \text{Na}^+ \rceil_0$ = or < 43mM. Lowering $\lceil \text{Ca}^{2+} \rceil_0$ with large reductions of $\lceil \text{Na}^+ \rceil_0$ can shift E_a into (-) region and abolish inward I_a . Hence, I_a is due to both N_a and C_a . I_b is due to K: when $\lceil K^+ \rceil_0$ = 120 or 149 mM, I_b is inwards in a voltage range which produced only outward I_b when $\lceil K^+ \rceil_0$ = 6 mM. E_b is very close to the resting potential and is readily influenced by the holding potential through passive redistribution of ions. I_a and I_b are both affected by passive redistributions, but on depolarization, both follow the Hodgkin-Huxley h type relation. I_b also declines with time. Chord conductances (g_a and g_b) vary exponentially with membrane potential. g_a is not affected by $\lceil \text{Na}^+ \rceil_0$ but is reduced by low $\lceil \text{Ca}^{2+} \rceil_0$. Epinephrine caused increased negativity of E_b , but does not affect any conductances. Its hyperpolarizing action is probably mainly metabolic associated with an increased uptake of K. (Supported by NIH grant HD 378)

852 VAGAL TONE IN HUMAN BEINGS. S.R.KAPOOR. G.S. V. M. Medical College, Kanpur, Uttar Pradesh, INDIA.

Degree of vagal tone was studied by determining the percentage increase in the heart rate after atropine injection in healthy male and female students and rickshawpullers. The average vagal tone was found to be $68.32\pm24\%$ in the male students, $57.73\pm20\%$ in the female students and $103.52\pm30.58\%$ in the rickshawpullers. It is concluded that physical exertion tends to increase the vagal tone, which is a quantitative measure of the degree of cardiac reserve and hence the efficiency of the cardiac muscle.

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URIC ACID-NEPHROPATHY IN SHOCK AND IN SHOCK-RESISTANCE. S. Karád, D. Boda, Á. Gecse, E. Zsilinszky, P. Pénzes. Institute of Pathophysiology and Pediatric Clinic, University Medical School of Szeged, Szeged, Hungary.

In rats with inhibited uricase activity by oxonic acid administration prior to the exposure to sublethal tourniquet shock, the uric acid level of the blood and kidney increased significantly, pronounced renal failure developed due to uric acid precipitation in distal tubuli /uric acid lower nephron syndrome/. In experiments carried out in the same way in rats previously rendered resistant to tourniquet shock, when subjected to sublethal tourniquet shock - inspite of the moderate rise in uric acid level of blood and kidney - did not develop any uric acid lower nephron syndrome and no renal insufficiency ensued.

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EVOLUTION OF INTEGRATIVE BRAIN FUNCTIONS IN SUBMAMMALIAN VERTEBRATES.

A.I.Karamyan and N.P.Vesselkin. Inst. of Evolutionary Physiology & Biochemistry Acad. Sci USSR, Leningrad, USSR.

Several species of submammalian vertebrates have been studied with electrophysiological, anatomical and behavioral methods. In Cyclostomes, neuronal responses and potentials evoked by stimulation of different sensory modalities are widely distributed over the brain. In Amphibia spezilized monomodal visual and somatic neurons are found in the tectum and in the thalamus, but seem to be absent in the telencephalon. The existence of the directe neothalamo-telencephalic projection has been demonstrated anatomically. Non-olfactory (visual and somatic) specialisation in the telencephalon first in phylogenesis arises in the neocortex of Reptilia. This thalamo-telencefhalic differentiation appears to be the basis for the experimentally demonstrated ability of the reptilian brain to elaborate complicated conditioned reflexes (associative reflexe and reflexe to complex stimuli).

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ELECTROPHYSIOLOGICAL ANALYSIS OF THE AVIAN FORE-BRAIN BIOELECTRICAL ACTIVITY UNDER THE CONDITIONS OF VARIOUS LIGHT-EXPOSURE. S.K.Karapetian. Orbeli Inst. of Physiology, Armenian Academy of Sciences, Yerevan, USSR. Several series of experiments were carried out by means of electrophysiological method to investigate the avian brain electrical activity under the conditions of various light-exposure. The following results were obtained: the brain activity parameters (frequency, amplitude & duration) were considerably increased under the prolongation of the natural daytime by 3-4 hours. When the birds after the prolonged light-exposure were transferred into complete (twenty-four hours) darkness there was observed extreme depression of brain activity. When after the complete (twenty-four hours) darkness the birds were kept again under natural day-time light conditions the intense change in brain phonic activity, expressed in the appearance of desynchronization EEG, was possible to observe after a month's period. The diffuse localization of the evoked responses on the light-flash was observed in other series of experiments. The results described prove the stimulating influence of the light on the avian brain activity.

RESPONSES OF BRAIN STEM RESPIRATORY NEURONES TO AFFERENT STIMULATION OF THE VAGUS NERVES. W.A. Karczewski. Lab.of Neurophysiology, Polish Academy of Sciences Med. Res. Ctr., Warsaw, Poland.

Unit activity of brain stem inspiratory and expiratory neurones, phrenic nerve discharges and end-expiratory CO, percent were recorded in spontaneously breathing and artificially ventifated rabbits whose vagus nerves were stimulated with various frequencies at constant, threshold intensity. High frequencies (100-1000 i/sec.) inhibited inspiratory and excited expiratory activity; low frequencies (20-40 i/sec.) produced an opposite effect. Triggering the pulse-generator by action potentials of a neurone itself ("self-stimulation") or by a single-fibre activity of the phrenic nerve invariably accelerated the respiratory rhythm in vagotomized animals. The effects depend upon the depth of anaesthesia. It is concluded that vagal afferents may exert a very complex influence on the respiratory "centres" of the brain stem.

857 DETERMINATION OF ELECTROPHYSIOLOGICAL PROPERTIES IN FROG SKIN W. Karger Inst. of Physiology Ruhr University Bochum W. Germany

The voltage/current/resistance relations in the isolated frog skin were investigated under different conditions. An analysis of the electrical network characteristics representing skin e.m. f. and permeabilities for active and passive ions was made in order to study deviations from linear behaviour at higher current loads. For a special experiment, the short-circuiting of a skin can be effected by another biological e.m. f. (instead of using an external battery): A circular array of four Plexiglas cells was set together with skins mounted in series, thereby forming a closed electolytic circuit. When administering bathing solutions with nearly impermeable anions, active sodium transport will go on through the skins round the circular pathway, so reducing the membrane potentials of those skins with originally lower voltage to even negative values.

858 LEFT ATRIAL RECEPTORS AND REFLEX CHANGES IN SYMPATHETIC EFFERENT IMPULSE ACTIVITY. F. Karim, C. Kidd, C.M. Malpus and P.E. Penna, Cardiovascular Unit, Department of Physiology, University of Leeds, England.

In dogs anaesthetized with chloralose, a study was made of the effects of distending the right pulmonary vein-atrial junctions by small balloons, on impulse activity in few fibre preparations from the right inferior cardiac nerve, the renal sympathetic nerves, the lumbar sympathetic trunk (below the origin of the renal artery) and splenic sympathetic nerves.

Balloon distension caused an increase in cardiac, a decrease in the renal and no change in the lumbar and splenic nerve activity. The cardiac and renal nerve responses were abolished by vagal blockade. The viability of lumbar and splenic strands was tested by occluding both common carotid arteries.

The results confirm the differential nature of the responses of the sympathetic nervous system to activation of left atrial receptors. In addition, they show for the first time an inhibitory effect on renal sympathetic nerve impulse activity; thus indicating that a neural factor, possibly involving renal haemodynamics, may be a component of the diuretic response to activation of left atrial receptors.

INTRATUBULAR TITRATABLE ACID, AMMONIA AND BICARBONATE IN RAT CORTICAL NEPHRON.

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Sweden.

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The characterization of renal tubular acid-base regulation should be expressed in terms of free (pH) as well as bound (TA + NH₄) hydrogen ions together with bicarbonate content. This is necessary in order to obtain a more adequate information on the total amount of acid (or base) transported across a given part of the renal tubular wall. But the determination of titratable acid in tubular urine presents significant methodological problems due to the minute samples available. A method will be presented which permits such a titration with high accuracy, and at the same time is usable for the determination of ammonium ions and bicarbonate ions in samples of about 1 nl. The method is coulometric with the use of antimony microelectrode systems for the pH measurements as well as for the alkalinization. By formal titration of the samples, it is further possible to determine the content of amino groups and ammonium ions. Equilibration with gases with known PCO₂ values permits calculation of the bicarbonate content. Titration curves will be automatically and simultaneously recorded. The method is designed for micropuncture studies on rat cortical nephrons, but could be used for most biological redox-free solutions – preferably nanoliter samples.

IACTATE METABOLISM IN MAN AFTER PROLONGED EXERCISE. <u>J. Karlsson and L. Jorfeldt, Dept. of Physiology</u>, Gymnastik- och Idrottshögskolan, Dept. of Clinical Physiology, Karolinska Institutet, Serafimerlasarettet, Stockholm, Sweden.

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A preceding period of prolonged heavy exercise has been shown to reduce blood lactate at standardized work loads. In order to clarify this phenomenon, young male subjects, given standardized bicycle work loads after preceding, prolonged exercise, were studied with respect to muscle lactate concentration (the quadriceps femoris) and the ability to utilize an infused lactate tracer. At a test load corresponding to 75% of max VO₂, blood lactate concentration was significantly reduced (30%) while muscle lactate concentration remained unchanged (11-14 mmoles x kg⁻¹ wet muscle). On the basis of these results and O₂ deficit calculations, it seemed reasonable to assume an enhanced utilization of blood-borne lactate induced by the prolonged exercise. Labelled lactate (1-C¹⁴ - lactate) was infused into the femoral artery during exercise in order to test this hypothesis. The fractional uptake was found to have increased by 40-50% as compared to control experiments. Moreover, significant amounts of C¹⁴ O₂ were found in venous blood draining the thigh. This all confirms the hypothesis of an unimpaired lactate formation at standardized work loads after prolonged exercise and an elevated utilization of blood-borne lactate by the working muscles, resulting in a decrease in blood lactate.

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EVOKED POTENTIAL CHANGES REFLECTING MOTIVATIONAL PROCESSES OCCURRING DURING INSTRUMENTAL LEARNING. G. Karmos, E. Grastyán and J. Martin.

Inst. of Physiology, Univ. Med. School, Pécs, Hungary.

Recently it was concluded by several authors that the modifications of

Recently it was concluded by several authors that the modifications of evoked potentials elicited by the conditioned stimulus during the learning process are primarily related to the information content of the signal. The aim of the present study was to test an alternative hypothesis, namely, that the modification of evoked potential waveshapes reflect nonspecific processes. In cats we analysed the changes of averaged cortical evoked potentials elicited by such click stimuli which were kept indifferent by applying them uninterruptedly during the whole course of elaboration of an instrumental avoidance conditioned response. The increase of illumination of the cage served as conditioned warning stimulus. It was found that also the potentials evoked by stimuli devoid of any definite signal importance show characteristic changes both in different stages of conditioning and in different phases of performance of the conditioned reactions. These changes could most probably be attributed to the fluctuation of the motivational level of the animal. The conclusion seems warranted that the evoked potentials elicited by the meaningful conditioned stimulus should also be complicated by these processes.

862 Exophthalmoradiographometry: A new technique for measuring eye protrusion in manR.M.Kassem, A.F.El-Zayat, M.A.Labib. Depts. of Physiology and Ophthalmology,
Al-Azhar and Cairo Universities, Cairo, U.A.R.

The aim of this study was to contrive a better technique for measuring eye protrusion in man than the prevailing ones. A plastic contact lens with a small central disc of lead is applied to the cornea. An x-ray film is taken for the skull in a good lateral position. On the film distances from anterior clinoid process to the cornea (A) and to the Nasion (B) are measured. An "Exophthalmic Index" i.e. A/B was found to be normal if it is 0.8-1.0. If it is more than 1.0 or less than 0.8 exophthalmos or enophthalmos is respectively diagnosed. The method is easy and its error is little compared to other known methods specially those using combined photographic and radiographic techniques. It is recommended for routine use in hospitals.

THE ROLE OF HUMORAL-HORMONAL INTERRELATIONS IN ESTIMATING THE TONUS AND REACTIVITY OF THE VEGETATIVE NERVOUS SYSTEM. G.N.Kassil. Lab. on Problems of Regul. of Functions in Human and Animal, USSR Academy of Sci., Moscow, USSR

Catecholamines, their precursors and products of metabolism, acetylcholine /free and bound by erythrocytes in vivo and in vitro/, histamine, histaminepexy, serotonin, 5-oxy-indolacetic acid, gluco-and mineralo-corticoids as well as some synthesizing and splitting ferments are determined in the blood, cerebrospinal rluid and urine of normals and patients with disorders of regulation of functions. The vegetative equilibrium is proved to proceed with the continious changing of the ratio of sympatho-and parasympathomimetic metapolits in the internal environment. Special functional tests dynamically estimating biologically active substances in the blood and urine have been worked out in order to prognosticate vegetative reactions. Cold, warm, adrenaline, insuline tests, administration of some pharmacological and hormonal agents are used. Shifts in the composition and biological properties of liquid mediums and organism excretions are found to precede physiological reactions. Depending on the type and course of the test these shifts allow a possible reaction of the sympathetic and parasympathetic sections of the vegetative nervous system to be provided for under normal and pathological conditions and to make necessary correctives in the development of physiological and pathological processes.

MELANOCYTE-STIMULATING HORMONE (MSH) RELEASE AND CNS EFFECTS. Abba J. Kastin, Curt A. Sandman, and Andrew V. Schally. Veterans Administration Hospital and Tulane and Louisiana State University Medical Schools, New Orleans, Louisiana, USA.

The release of MSH from the pituitary gland of mammals, like that of amphibians, is controlled primarily by an inhibiting factor (MIF) of hypothalamic origin. The evidence for this, obtained in the rat during the last 5 years, consists of the following: (1) decreased pituitary MSH content after pituitary transplantation, stalk section, or hypothalamic lesion; (2) increased pituitary MSH content after injection of hypothalamic extracts from several species, including a bovine preparation purified 11,000-fold; (3) decreased MSH activity in the medium of pituitaries cultured with hypothalamic extracts for 4 days; (4) decreased plasma levels of MSH after injection of MIF; (5) lightening of frogs, previously darkened by hypothalamic destruction, after injection of hypothalamic extracts; (6) growth of brown fur in weasels with pituitary autografts (Rust and Meyer) under conditions in which growth of white coats was expected. A hypothalamic MSH releaser (MRF) may also exist. Administration of MSH produces EEG changes in the frog, rat, rabbit, and human. Rats receiving MSH have facilitated reversal learning, perseveration of an appetitive response for food when hungry, and delayed extinction of responses for escaping (DeWied) and avoiding shock. Constant illumination and darkness, which affect pituitary MSH content (via the pineal gland and probably MIF), also modify some behavioral responses of rats to MSH. In summary, the hypothalamus inhibits the release of MSH, a pituitary hormone possessing extrapigmentary properties which may enable rats to respond adaptively.

A POSSIBLE MEDULLARY CHEMOCEPTIVE MECHANISM IN THE REGULATION OF CARDIOVASCULAR FUNCTION.

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College. Tokyo, Japan.

I Dept. of Medicine, Univ. of Tokyo, and Tokyo Women's Medical

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30 - 600 ng of angiotensin, Norepinephrine and isoproterenol was injected into the brainstem of chloralose-anesthetized cats using three-barrel chemitrode, in order to elucidate central sites of cardiovascular action of these agents. Diencephalon, midbrain and most of the poiss were not responsive to such stimuli. Pressor responses, rarely depressor ones, were obtained from microinjection of these drugs into the relatively restricted regions in the medulla, especially in the area postrema and its vicinity, but not from injection of mock CSF into the same area. Contraction of the nictitating membrane, bradycardia and respiratory inhibition were common features associated with these pressor responses. Pressor reactions were also observed in the vagotomized cats, and the responsive sites to electrical stimulation extended over more wide area in the lower brainstem. These evidences suggest that medullary chemoreceptors to angiotensin and catecholamines are separate from classically localized vasomotor center and integrate informations about a number of chemical changes for the regulation of cardiovascular function, presumably through sympathetic nervous mechanism.

EFFECTS OF DEITERS' NUCLEUS STIMULATION ON HINDLIMB FUSIMOTOR NEURONS IN CATS.

and J.Tanji Dept. of Physiology, Hokkaido Univ., Sch. of Med., Sapporo, JAPAN

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The effects of electrical stimulation of Deiters' nucleus upon hindlimb fusimotor neurons were investigated in 38 decerebrated and decerebellated cats. Fusimotor activity was recorded in ventral roots as well as in peripheral nerves. (1) among 61 fusimotor units recorded in the L7 and S1 ventral roots, 24 units(39.3 %) were facilitated, 11 units (18.0 %) were inhibited and no visible effect was observed on the remaining 26 units(42.6 %). (2) in the peripheral nerves 53 fusimotor units were investigated: 18 medial gastrocnemius, 5 lateral gastrocnemius-soleus, 7 tenuissimus, 19 semitendinosus, 3 anterior tibial and 1 plantaris nerves. Extensor fusimotor neurons such as medial gastrocnemius (4/18 = 22.2 %) and lateral gastrocnemius-soleus(3/5 = 60.0 %) were facilitated and flexor fusimotor neurons such as semitendinosus(9/19 = 47.4 %), tenuissimus(2/7 = 28.6 %) and tibialis anterior(2/3 = 66.7 %) were inhibited. (3) this reciprocal effects correspond to those of Wilson & Yoshida(1969) who obtained, on stimulation of the Deiters' nucleus, facilitatory effect on extensor alpha motoneurons and inhibitory effect on flexor alpha motoneurons. Apparently the facilitatory effect from the Deiters' nucleus upon extensor alpha motoneurons is strengthened by increased spindle afferent discharges from their own as well as from synergistic muscle spindles, and inhibitory effect upon flexor alpha motoneurons is supplemented by decreased sensitivity of flexor muscle spindles.

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By recording single nerve fiber responses to mechanical as well as chemical stimulation on the body surface, the lateral-line organs were studied of several aquatic animals; lampreys, sharks, teleosts and toads. Freestanding organs and pit organs, but not canal organs, were found to be sensitively responsive to monovalent cations, especially to potassium ions, some of them to mono-and divalent cations and some others to anions too, besides to mechanical stimuli. From those experimental results they can be said to have the dual functions, the mechano-and chemoreception. In aquatic animals the lateral-line organs may be a sensitive detector of salt concentration in the environment, namely the external salt taste organs. The lateral-line organ of the tadpole that has no tongue may play the role of the taste organ which is replaced during metamorphosis by the salt taste buds at the tip of the tongue. Furthermore their mechanosensibility were enhanced particularly by potassium ions in correlation with their concentrations. Those organs may therefore be designated as a better model of the inner ear of higher animals.

CHEMORECEPTION OF LATERAL-LINE ORGANS IN AQUATIC ANIMALS. Y. Katsuki,

and Dent. Univ., Yushima, Tokyo, Japan.

T. Hashimoto, N. Onoda and K. Yanagisawa. Dept. of Physiology, Tokyo Med.

ADH - INDEPENDENT WATER FLUX ACROSS THE SKIN OF TOADS, PREVIOUSLY ADAPTED TO HIGH SALINITIES. U. Katz, Dep. of Zoology, The Hebrew Univ. of Jerusalem, ISBAEL.

The toad Bufo viridis, can be adapted to live in NaCl solutions of up to 750 mOsm. The osmotic concentration of the plasma is always hypertonic to the medium. Water flux was studied in vivo and also in vitro using a preparation of the isolated skin, attached to a conus made out of perspex, and filled with hypotonic solution. It was found that the skin from high saline adapted toads is freely permeable to water; the addition of synthetic hormone, syntocinon, was of no further effect. In vitro bioassay, using bladders from animals living in tap water, failed to recover hydroosmotic activity higher than 5-10 pU/ml in the plasma of high saline adapted toads, (i.e. not distinguished from the activity found in plasma of animals living in either tap water or saline). The results show that a part of long term adaptation to high salinities of the toad Bufo viridis, is achieved by a change in the passive permeability of the skin to water, and is not mediated by neurohypophysial hormones.

SPONTANEOUS AND REFLEX ACTIVITY OF SINGLE UNITS IN LUMBAR WHITE RAMI. A. Kaufman,
K. Koizumi and C. McC. Brooks. Department of Physiology, State University of New York,
Downstate Medical Center, Brooklyn, New York, USA.

Spinal and supraspinal pathways have been shown to exist for somato-sympathetic reflexes, but information on these reflexes is very limited in mass recordings. Single-unit activity picked up from dissected white rami in chloralose anesthetized cats reveals that: (1) some preganglionic neurons can be activated through both pathways, and some through only one pathway; (2) both pathways can often be excited by stimulation of rapidly conducting afferent A-fibers; (3) the pattern of reflex activity was not strongly correlated with the degree of spontaneous activity; (4) in addition to the commonly observed late silent-period of spontaneous activity which follows the supraspinal pathway response, a low-threshold, early silent-period of spontaneous activity was sometimes seen following spinal pathway reflex discharges. This spinal pathway inhibition of sympathetic activity could be graded, and it interacted with the excitatory response. (Supported by USPHS Grant NS-00847-15).

CORRELATED CHANGES IN LH RELEASE AND ELECTRICAL ACTIVITY OF THE BASAL HYPOTHALAMUS INDUCED BY ELECTRICAL STIMULATION OF THE MEDIAL PREOPTIC AREA. M. Kawakami and E. Terasawa. Dept. of Physiology, Yokohama City Univ. Sch. of Med., Yokohama, Japan.

The effect of electrical stimulation (ES) of the medial preoptic area (MPO) on integrated multiple unit activity (MUA) in the arcuate nucleus (ARC) during the estrous cycle of the Wistar rat was examined with reference to the release of the ovulating hormone from the anterior pituitary gland. The ES (0.5 ms, 200 Hz, SW, 100-500 µA) was applied for 30 min between 14:00 to 16:00 under pentobarbital anesthesia. 1) When the stimulus induced ovulation on the following day, MUA changes in the ARC were observed during ES on the day of proestrus, in contrast to their appearance after ES on the day of diestrus II. 2) The ES facilitated the release of the ovulating hormone on the day of proestrus, while on the day of diestrus II it increased pituitary potency to ovulate as well. 3) The circulatory level of the luteinizing hormone (LH) elevated immediately after the ES, reached maximum level 30 min later and returned to the control level after 60 min on the day of proestrus. However, on the remaining days of the cycle it elevated immediately, reached maximum level at 60 min, but did not return to the control level even 120 min after the ES.

The differences of timing in responding to the ES of the MPO during the estrous cycle suggest neural excitation of the ARC producing synthesis and release of LH in the pituitary gland.

EFFECTS OF TETRODOTOXIN ON PERISTALSIS AND ACETYLCHOLINE OUTPUT. T. Kažić. Inst. of Pharmacology, Faculty of Medicine, Belgrade, Yugoslavia

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Tetrodotoxin (TTX) has been known to abolish the action potentials, thus preventing inward movement of sodium ions, and consequently to prevent acetylcholine (Ach) output from the stimulated nerves. Motor responses of the gastrointestinal tract mediated by nerve stimulation have also been blocked by TTX. Increase of the intraluminal pressure was shown both to elicit peristalsis of the isolated guinea-pig ileum, and to produce many-fold increase of the acetylcholine output.

These experiments were done in order to correlate the effect of TTX on

These experiments were done in order to correlate the effect of TTX on the peristalsis with the effect on the Ach output, i.e. to test the hypothesis that Ach_plays a major role in peristalsis.

TTX (2 x 10 g/ml) was found to block peristalsis preventing only the emptying phase, and to abolish the Ach output due to increased intraluminal pressure. Both effects were reversible and their patterns of recovery ran parallel in the course of a longlasting recovery period.

These findings are taken as supporting the idea that Ach released due to increase of the intraluminal pressure in the gut plays a role of the major transmitter substance in the peristaltic function.

major transmitter substance in the peristaltic function.

ELECTRICAL AND MECHANICAL RESPONSES OF ARTERIAL SMOOTH MUSCLE IN Ca-FREE SOLUTIONS. W. R. Keatinge. Physiology Dept., London Hospital Medical College, London, England.

When arterial smooth muscle was placed in Ca-free saline containing EDTA (1.25 - 12.5 mM) its membrane potential fell. Application of noradrenaline (0.1 mM) then caused contraction as it does in physiological saline containing Ca, but with repolarization of a few millivolts instead of the depolarization seen in Ca-containing solutions. These electrical changes were recorded in sucrose-gap apparatus. After many minutes in EDTA at the arteries lost all electrical responsiveness to noradrenaline, and later lost their mechanical responsiveness. The rate of loss of mechanical responsiveness in such solution became extremely slow when the temperature was reduced to 5°C ; the arteries contracted in response to noradrenaline when warmed after 1 hour in EDTA at 5°C . The results suggest that noradrenaline could activate contraction by means not dependent on extracellular Ca or on electrical activity of the cell membrane.

ELECTROPHYSIOLOGICAL ANALYSIS OF THE EFFECT OF CELLULINE-A IN CARDIAC PREPARATIONS. Valéria Kecskeméti.K. Kelemen, J. Knoll. Dept. of Pharmacology, Semmelweis Medical School, Budapest, Hungary.

Celluline-A markedly changed the transmembrane potentials of the frog's

ventricle and cat's auricle. A significant increase of the rate of rise and the overshoot has been observed in baths of physiological ionic composition, as well as in the presence of slight potassium excess or sodium lack. These changes occured without any shift of the resting potential. In the presence of high external potassium concentrations /25-30 mM/ celluline-A restored the mechanical and electrical activity of the heart preparations at the unchanged; lowresting potential level /38-45mV/ characteristic of the given potassium excess. The data render indirect evidence that under the influence of celluline-A sodium permeability of the heart cell membrane is significantly increased.

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RESPONSE OF THE CARDIAC CONDUCTION SYSTEM TO ACUTE RESPIRATORY ARREST.

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Ramat Gan, Israel.

Experiments were performed in open-chest, nembutal anesthetized dogs in which atrial and standard lead electrocardiograms were measured. The refractory period of the A-V node was estimated by delivery of premature atrial stimuli and determination of the shortest R-P interval which elicited a QRS complex. Such determinations were made before, during, and following periods of tracheal occlusion. It was found that acute apnea produced a marked sinus bradycardia, accompanied by a significant prolongation of the refractory period, but an only slightly prolonged P-R interval. Atropine blocked the appearance of sinus bradycardia as well as the increased R-P interval. The P-R interval was markedly lengthened during hypoxia induced after pretreatment with a ganglion blocker, while the refractory period remained unchanged. Pronethalol further lengthened the P-R interval whereas the R-P interval was shortened. It is concluded that the conduction velocity and refractoriness of the A-V node can be distinguished during hypoxia; whereas nodal conduction time is shortened by adrenergic mechanisms, refractoriness is probably not similarly influenced.

875 ANTAGONISM BETWEEN TOTAL BODY FAT AND BODY SURFACE AREA TO VOLUME RATIO IN BODY COOLING AT 15 C. Kee Yong Nam and Kwan Ogg Chung. Dept.of Physiology, Seoul Natl.Univ.Col.of Medicine, Seoul, Korea.

Skin temperatures on 10 sites and rectal temperature at every 10 minutes were measured on 18 men for 2 hours in a climatic room at 15 C. Total body fat was calculated through the skinfold thickness at 4 sites. Body surface area (S) was obtained by the DuBois equation. Body volume (V) was determined by underwater weighing. The influence on the heat loss from the body core to the cold environment of the antagonism between %fat and S/V ratio was demonstrated by observations as follows: minimum rectal temperature was higher in fat subjects (r=.60) and lower in subjects with a greater S/V ratio (r=.58). ATR was smaller in fat men (r=-.74) and greater in men with a greater S/V ratio (r=.62). Temperature difference between body core and skin surface (minimum rectal temperature minus minimum mean weighted skin temperature) showed a positive correlation with %fat (r=.60) and a negative correlation with S/V ratio (r=-.88). Decrease in the mean body temperature and heat debt, respectively, showed negative correlations with %fat and positive correlations with S/V ratio.

876 PECULIARITIES OF THE SELF-RENOVATION CYCLE. P. Kehayov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

A complete self-renovation cycle was experimentally obtained and the peculiarities of its phases of fatigue, recuperation and exaltation were investigated. The study was made by a specially constructed ergograph. A method for determining the state of the working organ through the ergographic patterns is described. Considerable attention is devoted to the activation, the fatigue as a feed-back, the different in magnitude loadings and particularly the overloading, and to their effect on the run of the self-renovation cycle. Studies in detail were made on the phase of exaltation as a natural end of the self-renovation cycle and on the peculiarities of its run being of general character or related to the preceding loading.

PHARMACOLOGICAL ANALYSIS OF A TIO-COMPONENT DEPOLARIZING RESPONSE IN APLYSIA NEURONES JacSue Kehoe. Lab. Neurophysiol. Cell., CMRS, 91, Gif sur Yvette, France.

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The pre- and postsynaptic neurones of a group of non cholinergic synapses have been identified in the pleural ganglion of the Aplusia. Activation of the presynaptic neurones causes a two-component depolarizing response consisting of a rapid EPSP and a slowly developing depolarization. Neither ACh, GABA, dopamine, nor serotonin appear to play a transmitter role at this synapse. Although each has a distinctive action on the postsynaptic cells, their effects can be selectively blocked without affecting the twocomponent depolarization.

Glutamate, likewise, does not appear to be the transmitter involved since it causes a postsynaptic hyperpolarizing response. It has been noted, however, that glutamate causes a marked reduction of the rapid phase of the input as well as a marked potentiation of the slow component. These effects are reversible, and can be obtained by using either the D or the L form. These actions of glutamate are shared by aspartate and butyrolactone, but are not shared by the following compounds having neighboring structures: glutamine, glutaric acid, asparagine, and propiolactone. The active compounds have no effect on four other identifiable synantic inputs to the same group of postsynantic cells.

ANALYSIS OF PERMEABILITY CHANGES CAUSED BY CELLULINE-A IN CARDIAC TISSUE.

ANALYSIS OF PERMEABILITY CHANGES CAUSED BY CELLULINE-A IN CARDIAC TISSUE.

K.Kelemen, Valéria Kecskeméti, Józsa Skolnik, J.Knoll.Dept.of Pharmacol.

Semmelweis Medical School, Budapest, Hungary.

Indirect electrophysiological evidence indicated that celluline-A
increased the sodium permeability of the heart cell membrane.Direct
flux measurements showed that the rate of Na-exchange of frog ventricle
and cat auricle loaded with Na and perfused with inactive solutions
is doubled under the effect of celluline-A even in the presence of
ouabain /10-5/. Furthermore, celluline-A was capable to restore the
activity of heart preparations poisoned with high doses of either tetrodotoxine /10-7/ or manganese ions /4 mM MmClp/, but failed to act in
the presence of both TTX and MmCl2. The data indicate that under the
effect of celluline-A the conductivity of both the TTX-sensitive fast
Na-channel and the Ma-sensitive slow /possibly Ca/ channel is enhanced,
so that either of them can substitute for the complete blockade of the
other. This provides further evidence that, in the heart cell membrane,
celluline-A interferes with the process of transformation from the
resting state to excitation. resting state to excitation.

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A PNEUMATIC SYSTEM FOR ANALYSIS OF ELE MOVEMENTS IN PSICHO-PHISIOLOGICAL EXPERIMENTS. L. Kellényi, W.G. Walter and R. Cooper. Med. Univ. of Pécs. Inst. of Physiology, Hungary and Burden Neurological Institute. Bristol, England.

The relation between the periodic eye movements and the occipital BEG activity is still an unsolved problem. One of the basic difficulty of the study of this problem is the exact registration of the movements of the eye balls. In the present paper a pneumatic system is described for this purpose. The receptor is attached to an eyeglass frame and consists of a 16 mm. diameter prespex tube the end of which is closed with a thin ruber

membrane. During the experiments the membrane gently lies on the closed eye. The pressure changes on the receptor is detected by a sensitive capacitance micro-pressure transducer. The voltage output of the system can directly be connected to one channel of the EEG maschine. This simple method was found to be useful for the accurate registration of eye movements.

B80 DIURNAL VARIATION IN SKIN BLOOD FLOW AND VASOMOTOR ACTIVITY IN MAN.

E.Kellerová, M.Kittová, Institute of normal and pathological physiology,

Slovak Academy of Sciences, Bratislava, Czechoslovakia.

In 11 healthy subjects skin blood flow /BF/,blood pressure /BP/,heart rate and skin temperature were recorded at 3 hr intervals, between 9 a.m. and 9 p.m. All these parameters were followed at rest and during adrenergic reactions /to the deep breath and to mental arithmetics/. In the course of the day,regular variations of BF and peripheral vascular resistance /PR/ in skin were demonstrated. At rest the peak BF was observed in skin at 9 p.m., minimal at 6 p.m. Mean values for PR decreased in the evening by nearly 50 % in comparison to the values found at noon or at 6 p.m. The mean BP did not change to any considerable degree during the day. The skin temperature rose significantly at 3 p.m., with acral skin temperature showing fluctuations depending on changes in BF. The vasoconstrictor reactivity to the above mentioned stimuli, expressed in the terms of BF and PR was found to be maximal at 9 a.m. and at 9 p.m. There are two minima of vasomotor reactivity in skin, at noon and at 6 p.m. The lowered vasomotor reactivity to adrenergic stimuli might be taken into account as one factor of cardiovascular lability observed at noon in other test situations by other authors /e.g. orthostasis/.

PROLONGATION OF THE INHIBITORY RESPONSE OF CORTICAL NEURONES TO SYNAPTIC STIMULATION AS A RESULT OF DELAYED GABA INACTIVATION. <u>John S. Kelly and Leo P. Renaud</u>. Anaesthesia Research, McGill Univ., Montreal, Canada.

Amino-oxyacetic acid (AOAA) caused a pronounced increase in the intensity and duration of the inhibitory response evoked by electrical stimulation of the cortical surface and pyramidal tract and by small applications of GABA by iontophoresis. In 12 experiments, the inhibitory effects on a single neurone of the cat pericruciate cortex were observed, at frequent intervals during a control period and after the injection of 20-40 mg/Kg i.p. of AOAA. Post-stimulus latency histograms were used to measure the reduction in the background neuronal discharge which was evoked by the iontophoretic release of glutamic acid. In order to counter the depressant action of AOAA the frequency of the background discharge was maintained at the control level by increasing the release of glutamic acid. Accentuation of the inhibitory responses to both exogenous GABA and synaptic stimulation is thought to be the result of delayed GABA inactivation and supports the suggestion that GABA is a central transmitter. The delayed inactivation of GABA may not be the direct result of the inhibition of GABA transaminase activity by AOAA but a consequence of the saturation of either binding or uptake sites. (Supported by the MRC of Canada)

STUDIES ON SINUS ARRHYTHMIA. G.R. Kelman and K.T. Wann, Department of Physiology, University of Aberdeen, Scotland. U.K.

We have measured, with a beat-by-beat cardiotachometer, the heart rate response to constant-volume pulmonary ventilation at varying frequencies. Subjects breathed, via a one-way valve unit and CO2 absorber to and from a spirometer containing oxygen. The subject was required to keep the spirometer volume between fixed upper and lower limits while breathing approximately sinusoidally at either 3, 4, 5, 6, 7½, 10 or 15 breaths/min. The amplitude of the arrhythmia varied with the ventilatory frequency. This amplitude was minimal at high frequencies, and maximal in the region of 5 or 6 breaths/min. The phasic relationship between lung volume and heart rate was likewise dependent on ventilatory frequency. Maximal heart rate coincided with the peak of inspiration when the ventilatory frequency was about 8 breaths/min. At lower frequencies the maximal heart rate occurred before inspiration was complete; at higher frequencies it lagged behind inspiration. In one subject we measured, via an intra-arterial cannula, radial artery pressure at varying ventilatory frequencies. The phase relationship between lung volume, heart rate and arterial pressure will be discussed.

EVIDENCE AGAINST A ROLE OF PARATHYROID HORMONE IN ADAPTATION TO LOW CALCIUM INTAKES. J.R.Kemm, Dept. of Physiology, University of Newcastle upon Tyne, England.

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% Apparent absorption [(dietary intake - faecal excretion) x 100 \div dietary intake] of Ca was determined by a balance study in albino rats six weeks after weaning. During the balance study each animal was given 10 g of a low Ca diet (0.2% Ca; 0.26% P) and during the preceeding six weeks the animals were fed the same diet ad lib. except for certain weeks when some of them were fed a high Ca diet (1.6% Ca; 1.6% P). All diets contained adequate Vit. D. The greater the number of weeks that the animal had been fed the high Ca diet the less was its apparent absorption of Ca, but there was no consistent trend in serum Ca. % Apparent absorption was found to be strongly correlated with % total carcase Ca (total carcase Ca x 100 \div carcase wt.).

% apparent absorption = $186 - (125 \times \% \text{ total carcase Ca})$ R = 0.768 52 observations

but there was no correlation between % apparent absorption and serum Ca. In this case one cannot invoke decreased secretion of PTH to explain the fall in apparent absorption unless one makes the additional hypothesis that its secretion may be controlled by some factor other than serum Ca and we may conclude that some mechanism other than reduced secretion of PTH is causing the fall in apparent absorption.

TELEMETRIC SYSTEM FOR STUDY OF CARDIOVASCULAR DYNAMICS IN UNRESTRAINED ANIMALS. S.Kemper, T.Patrick, S.Vatner, C.Higgins, D. Franklin. Scripps Clinic & Res. Fndn., and UCSD Med. Sch., La Jolla, Cal., U.S.A.

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Concepts of cardiovascular control are based mainly on studies in anesthetized animals It is probable that control mechanisms so identified are emphasized in a significantly different manner in normal conscious animals. We have developed radio telemetry measuring systems to monitor cardiovascular responses of unrestrained animals during spontaneous activities, e.g., exercise. The miniaturized system employs a Doppler ultrasonic blood flow meter for measurement of multiple flows and an implantable pressure gauge for measurement of ventricular or aortic pressure. These signals are radio transmitted with an FM/FM telemetry system. A miniature radio interrogation system controls power, flow measuring site, and neural stimulation remotely. The system measures regional flows (coronary, renal superior mesenteric, iliac) and pressures in animals totally unrestrained and uninfluenced by a laboratory environment. Thus, descriptions of the normal cardiovascular adjustments to various activities can be derived. For example, contrary to traditional concepts based on anesthetized animal experiments, a sustained decrease in visceral flow does not occur during vigorous spontaneous exercise in normal dogs. This system provided a first description of coronary dynamics in unrestrained higher primates. In addition, fundamental differences have been found between the anesthetized and the normal animal in the response to both carotid sinus stimulation and digitalis glycosides.

SPINAL REFLEX MECHANISMS IN THE LIZARD. P. Kenins, A.K. McIntyre and U. Prosec. Dept. of Physiology, Monash University, Victoria, Australia.

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Little is known about spinal reflexes in reptiles, in contrast to their extensive documentation in mammals. This report describes experiments on such reflexes in the blue tongue lizard, Tiliqua Nigrolutea. Tension developed in a hind-limb muscle was measured during its extension by different amounts above resting length, the limb being denervated except for the muscle under study. Length-tension plots before and after severing the muscle nerve or dorsal roots (D.R.) revealed the presence of an active stretch reflex. Single shock stimulation of D.R. evoked asynchronous reflex discharge in mixed nerves, usually of long (5-9 msec) latency. Intracellular recording from motoneurones revealed that most synaptic excitation by D.R. volleys was polysynaptic in origin. The depolarizing synaptic potentials showed successive steps indicating the arrival of increasingly delayed interneuronal input. Some, but not all, cells showed an early probably monosynaptic phase of depolarization. Motoneurone firing under these conditions usually took place in polysynaptic tempo; only rarely, as after a conditioning tetanus, could early, monosynaptic discharge be seen in response to a single D.R. stimulus.

886 EFFECT OF CHANGES IN PULMONARY BLOOD FLOW ON VENIOUS ADMIXTURE AND RIGHT TO LEFT INTRAPULMONARY SHULT FLOW IN DOGS. D. Kentera, V. Veljković, and D. Sušić, Inst. for Med. Res., Belgrade, Yugoslavia.

Venous admixture and right to left intrapulmonary shunt flow were studied at two different levels of perfusion through pulmonary artery. Experiments were done on spontaneosly ventilated dogs in chloralose anaesthesia. Pulmonary blood flow was controled by perfusion of different amounts dogs own blood, with help of a pulsatile pump. Level of blood flow was contineusely monitored by a rotametar and measured by direct Fick method. Venous admixture was expressed as a ratio of endcapillary-arterial and endcapillary-mixed venous blood differences in hemoglobin saturation, as calculated from pO, determined by Clark's electrode. Shunt flow was determined as venous admixture during pure oxygen breathing. Results obtained suggest that increase in pulmonary perfusion rises pulmonary shunt flow only when large enough to cause precappilary pulmonary hypertension of moderate degree.

887 INITIAL ADAPTATION OF FIRING RATE IN A NEURONE MODEL BASED ON 'VOL-TAGE CLAMP EQUATIONS'. D. Kernell and H. Sjöholm. Nobel Institute for Neurophysiology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden.

The present neurone model is based on the Frankenhaeuser-Huxley equations (J. Physiol. (Lond.) 171, 302, 1964) for voltage clamp data from the amphibian peripheral nerve. The calculations were made with a digital computer. The potassium system was modified so that an action potential was succeeded by a prolonged after-hyperpolarization (AHP) similar to the one seen in cat alpha motoneurones. Changes were also made in constants of the equations for sodium inactivation, and the membrane time constant was 5 msec. This neurone model responded with a repetitive impulse discharge to stimulation by a constant current. Firing rate varied with current intensity over a wide range. Essentially the same AHP could be produced with several different combinations of constants in the equations for the potassium system responsible for the AHP. With one set of values there was a marked 'summation' of the AHPs following consecutive spikes, and the model then showed a marked initial adaptation of firing rate just after the abrupt onset of a constant stimulating current. With another set of values, there was practically no 'summation' of AHPs and virtually no initial adaptation of firing rate. These results suggest that a 'summation' of potassium permeability changes underlying the AHPs of consecutive spikes may be of great importance for the initial phase of adaptation of firing rate in central neurones.

THE ROLE OF HISTAMINE IN THE REGULATION OF CARBONIC ANHYDRASE ACTIVITY P.Keszler, T.Gáti, T.Zelles, E.Pintér, Inst. of Pathophysiology, "Semmelweis" Univ. of Med., Budapest, Hungary

The role of both histamine and carbonic anhydrase in the gastric secretion is well known. In the present study distribution of carbonic anhydrase activity and of mucosal histamine content were investigated in the lesser- and greater curvature and pylorus of stomach in rats. The mentioned parts of stomach of the fasted /for 12 hr./ animals were homogenized and the activity of the enzyme colorimetrically and histamine content fluorometrically determined. Histamine content and carbonic anhydrase activity of the examined areas were different, but correlations have been found between histamine contents and enzyme activities.

The activation of carbonic anhydrase by histamine "in vitro" was also examined on starved or fed rats. The degree of histamine-activation was small in the first minutes of feeding and increased considerably

an hour later.

These results indicate that histamine plays an important part in the regulation of carbonic anhydrase activity of the gastric mucosa.

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HISTAMINE CONTENT OF NORMAL FEMALE HUMAN NASAL MUCOSA WITH SPECIAL REFERENCE TO MEN-STRUAL CYCLE. A.H.Khalifa and A.M.Geumei. Dept. Otolaryngology, Karmous Hosp. and Dept. of Pharmacology, Med. Sch. Univ. of Alexandria. U.A.R.

Histamine content of nasal mucosa (H) of 45 healthy female subjects between 4 and 43 years of age was estimated with the bioassay procedure using isolated guinea pig intestine. There was a wide variation in H with a mean value of 19.8±1.9½/g wet wt. Below 12 years of age (before puberty) the mean H was 16.4±2.3½, while that after 12 years (after puberty) was 21.8±2.1½/g wet wt. In a group of 6 female subjects between 18 and 26 years of age H was estimated at premenstrual, menstrual and postmenstrual periods. The highest mean value of histamine content was found during the premenstrual period (32.1±3.4½/g wet wt), the lowest during menstruation (18.9±1.3½/g wet wt). At postmenstrual period it was 20.9±1.8½/g wet wt.

In conclusion, histamine content of normal human nasal mucosa is affected by age as well as by the menstrual cycle.

NEURONAL MECHANISMS OF CONDITIONING IN INTACT AND ISOLATED CORTEX.
M.M.Khananashvili.Pavlov's Physiol.Dep.,Inst.Exper.Med.,Academy of Med.
Sciences, Leningrad, USSR.

Investigation of background spike cortex activity isolated from subcortical synapse influence is represented, as well as neuronal organization of "temporal connection" induced by simultaneous electrical stimulation of the isolated cortex. Chronic experiments were carried out in cats. Spike activity was registrated extra-cellularly. The investigation at different postoperative terms showed that the level of background spike activity of the isolated cortex gradually restored. It did not reach its preoperative level, however, even some weeks after the isolation. In the isolated cortex all types of background spike activity essential for the intact cortex retained. Neuronal reaction patterns to the direct electrical stimulation, peculiar for the intact cortex, were preserved, as well as "late trace dischages". As a result of simultaneous stimulation of 2 areas in the isolated cortex, it was stated that neurons became mutually conditioned. Such "temporal connection" retains for many minutes and can be a model for short-term trace phenomena in the cortex.

INTRACELLULAR POTASSIUM AND THE ELECTRO-CHEMICAL PROPERTIES OF STRIATED MUSCLE FIBERS. R. N. Khuri, Department of Physiology, American University of Beirut, LEBANON.

Uncertainty exists regarding the state of intracellular K⁺ and its effect on electro-chemical properties of excitable cells. In this study intracellular K⁺ activity and the resting membrane potential of single muscle fibers of the frog Sartorius were measured simultaneously in situ and in vitro. The intracellular K⁺ activity was measured by means of K⁺-selective liquid ion-exchange microelectrodes built as a single unit in a double-barreled configuration. The K⁺:Na⁺ selectivity of the cation-exchanger was 90:1. Cell K⁺ was measured by flame photometry and the extracellular space was determined with inulin-Cl⁺. In the in situ studies the mean K⁺ activity per kg of cell water was 105+0.7 (potentio-metric) as compared to a mean K⁺ concentration of 142+2.3 (Photometric). The resulting mean activity coefficient is 0.744+0.005, a value which is not different from that of simple solutions. In this study both the membrane potential and the K⁺ equilibrium potential were derived from simultaneous potentiometric measurements. The measured membrane potential mean value of 89+0.3 is quite close to the calculated K⁺ equilibrium potential mean value of 91.4+0.2. These results confirm that K⁺ is in electro-chemical equilibrium across the muscle fiber membrane.

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892 EFFECTS OF EXOGENOUS ATP ON GASTRIC ACID SECRETION. George W. Kidder III. Biology Dept., Wesleyan Univ., Middletown, Conn., USA.

The addition of ATP to the serosal bathing solution of from gastric mucosa in vitro produces changes in acid secretory rate, potential difference, and cytochrome c redox steady state. ATP (but not ADP or adenosine) causes a transient stimulation of secretion (~10 min. duration). This might be considered evidence for an ATP-driven pump; however, ATP cannot support secretion under anaerobic conditions. Further, both ATP and ADP, after 1 hr. incubation, increase the lag between return to aerobic conditions and the onset of secretion from its normal 6.5 min. to ~23 min. at 10 mM ATP. Tissues loaded with ATP from the serosal surface release inosine upon wash-out, showing that an adenyl compound entered the cells to gain access to the deaminase, and allowing measurements of the rate of adenyl entry. The data can be explained by a model in which acid secretion is driven by an electron transport system, in parallel to the mitochondrial system and competing with it for substrate. ATP would stimulate secretion by inhibiting mitochondrial oxidation, allowing more substrate for the secretory pathway. The lag increase is due to the longer time required for mitochondrial phosphorylation of the increased ADP, and consequent reduction in mitochondrial respiration. This model also accounts for the failure of added ATP to stimulate acid secretion under anaerobic conditions.

- 893 EFFECT OF OUABAIN ON ELECTRICAL RESPONSE OF VISUAL CELL OF HORSESHOE CRAB, <u>Tachypleus</u> tridentatus. <u>Ryoji Kikuchi</u>. Dept. of Physiology, Tokyo Women's Med. Col., <u>Shinjuku</u>, <u>Tokyo</u>, <u>JAPAN</u>.
 - (1) After the hyperpolarization caused by iron group divalent cations had reached a certain steady level, the resting membrane potential and response to illumination were diminished by addition of ouabain into the external horseshoe crab Ringer. (2) By a Ringer containing ouabain in addition to divalent cations, the induced hyperpolarization was less and hyperpolarizing phases appeared before and after the depolarizing phase of the response. Their amplitudes were changed in proportion to the intensity and polarity of the applied direct currents through the recording microelectrodes filled with potassium ferricyanide. (3) Replacement with a sodium-free ouabain Ringer had little effect on the resting potential and induced a reduction in the amplitude of the response and abolished spike potentials. Further substitution with an ouabain Ringer caused depolarization and the recovery of both the response and spike potentials.

These results seem to support the view that the electrical response of the visual cell in the lateral eye of the horseshoe crab is not due to the inactivation of a sodium-pump but to the conductance change of two kinds of ions, presumably sodium and potassium.

894 SLEEP PATTERN OF HIPPOCAMPECTOMIZED CAT. C. Kim. Dept. of Physiology, Catholic Medical College, Seoul, Korea

To see if the hippocampus has any influence upon sleep mechanism, cats that had more than 90% of their hippocampal tissue removed bilaterally through the cerebral cortex were prepared, and their EEG, E4G and EOG were recorded for 24 h before and following surgery.

(1) Hippocampectomy reduced the total time occupied by sleep, increased occurrence of sleep state (defined as a sequence of slow wave sleep or/and fast wave sleep phases between two successive awake states), and reduced mean duration of sleep state all significantly. (2) Circadian variation of sleep was preserved after hippocampectomy.

The hippocampus was inferred to be conducive to the maintenance of sleep.

STUDIES ON ENERGY EXPENDITURE OF KOREAN SERVICE PERSONNEL. D. J. Kim. Dept. of Physiology, Ewha Womans Univ. Col. of Med., Seoul, Korea.

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The studies were carried out on 176 persons ranging in age from 20 to 50 years to determine the basal metabolic rates, energy expenditure of various activities by Douglas' bag and Scholander's gas analyzer, and the daily energy expenditure using a record of their activities throughout 24 hours of every survey day. The greatest increase in ratio of energy expenditure in the basis of resting metabolism was 277.3% in floor mopping, and the least was 40.9% during hair cutting by beauticians. The assessment of daily energy expenditure of waiters is 3301 Cal, waitresses 2302 Cal, guards 3130 Cal, cooks 2993 Cal, cooks(F) 2680 Cal, bell boys 2781 Cal, drivers 2720 Cal, desk clerks 2630 Cal, file clerks 2335 Cal, file clerks(F) 1955 Cal, shoe-shine boys 2562 Cal, barbers 2527 Cal, janitors(F) 2986 Cal, laundresses 2924 Cal, room maids 2608 Cal, typists 2341 Cal, beauticians 2267 Cal, room service personnels(F) 2219 Cal and elevator operators(F) 1873 Cal respectively. In respect to the daily energy expenditure, most of the occupations are moderate or light work. But the janitor(F), laundress and room maid do heavy work.

MECHANISM OF INCREASED DIAMINE OXIDASE (DAO) ACTIVITY IN PREGNANCY. K. S. Kim and M. E. Harris. Dept. Pharmacology, The George Washington Univ., Washington, D.C. 20005, USA

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Factors influencing uterine DAO activity were studied in order to elucidate the mechanism of the increased DAO activity in pregnancy seen in man and rodents. In normal female rats, DAO activity of the uterus was very low but underwent a cyclic variation, increasing during estrus and decreasing during diestrus. Administration of estrogen (E), but not progesterone (P), increased uterine DAO activity in ovariectomized (OVX) rats. Intrauterine foreign body (IUFB) increased uterine DAO activity in OVX rats, which was however inhibited by E but greatly stimulated by P administration. An increase in total uterine and plasma DAO activity similar to that seen during pregnancy was obtained in OVX rats by daily administration of P provided IUFB was inserted on the 5th day of P treatment. These findings suggest that increased DAO activity in pregnancy is brought about by implantation of the blastocyst (acting unspecifically as IUFB) in the uterus which is primed and maintained by progesterone from the corpus luteum. In addition, uterine DAO activity in response to progesterone along with IUFB displayed a dose response relationship in OVX rats. This provides a basis for a highly sensitive progestational activity assay. This study also suggests that the antifertility activity of estrogen (postcoital) may be related to its inhibitory action on uterine DAO activity. E: estradiol be 2 µg/rat/day; P: 2 mg/rat/day in oil; Substrate for DAO assay: 14C putrescine. E: estradiol benzoate in oil 0.2 or (Supported by USPHS Grants GM-13749 and GM-26)

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INTERACTION BETWEEN SUGAR AND AMINO ACID TRANSPORT IN ISOLATED INTESTINAL EPITHELIAL CELLS G.A. Kimmich. Dept. Rad. Biol. & Biophys. Univ. Rochester Med. Center, Rochester, N.Y. A number of investigators have observed moderate mutual inhibition between active transport processes for sugars and amino acids in intact intestinal tissue. We have been able to show a more significant interaction in isolated intestinal epithelial cells. As an actively transported sugar is increased in concentration in the incubation medium there is progressively greater inhibition of active valine accumulation. At 10 mM galactose the transport of 1 mM valine is inhibited by 75%. Phlorizin completely relieves the sugar induced inhibition. The inhibitory effects are reciprocal in that actively transported amino acids induce a similar inhibition of sugar transport. Normal cellular sodium gradients are decreased by only 20% by 10 mM galactose. Furthermore, if a sugar which is both actively transported and rapidly metabolized is used, it can be shown that as much as 50% inhibition of valine accumulation may occur with no detectable collapse of the sodium g radient. These latter facts are inconsistent with predictions based on the sodium gradient hypothesis. The observed interaction is not due to competition for energy directly at the level of ATP as there is no detectable decrease in cellular ATP concentrations when amino acid transport is as much as 50% inhibited by galactose. Competition for a multi-functional carrier seems unlikely in that we are unable to demonstrate countertransport effects between the two substrate groups. An interpretation will be presented, consistent with our recent proposal that energized intermediates of [Na+ K+] ATP-ase may provide energy for several energy dependent events. Supported by U.S. Atomic Energy Comm. Report No. UR-49-1386.

STIMULATION OF RESPIRATORY CENTER BY MUSCLE STRETCHING AT DIFFERENT
ARTERIAL CO TENSIONS. W. Kindermann, K. Pleschka. W.G. Kerckhoff-Institut
der Max-Planck-Gesellschaft. Bad Nauheim. Germany.

der Max-Planck-Gesellschaft, Bad Nauheim, Germany.

The effect of arterial CO₂-tension (PaCO₂) on the ventilatory response to passive muscle stretching was studied in anesthetized, paralysed and artificially ventilated dogs with bilateral vagotomia. The integrated electrical activity of the phrenic nerve bursts and their frequency were used to estimate the reaction of the respiratory center. The gastrocnemius muscle was stretched by means of the piston-rod of an airmotor. At normal PaCO₂ the pattern of the phrenic nerve bursts during muscle stretching was equal to that previously observed in individual phrenic motoneurones under the same conditions (1). Accordingly, muscle stretching caused a significant increase of respiratory frequency and a smaller increase of integrated electrical activity of the single bursts. Both at higher and lower PaCO₂ levels, the change of inspiratory activity during the muscle stretch was the same, in principle, as at normal PaCO₂. Only the rise of respiratory rate was somewhat reduced. Since respiratory activity was elicited by muscle stretching also during apnea induced by hyperventilation it is suggested that stimulation of the respiratory center by activation of limb receptors is independent of PaCO₂. (1) K. Pleschka, K. Bock, W. Kindermann: Experientia 26: 856, 1970.

RECOVERY AND CONDITIONING IN ISOLATED FOREBRAIN. F.A. King, W.R. Fowler, and L. Roberts. Univ. of Florida College of Medicine, Gainesville, Florida, USA 32601.

Chronically maintained midbrain-transected cats eventually develop long-lasting episodes of low-voltage fast EEG activity in the forebrain. In view of the recognized imperfect correlation between EEG and behavioral arousal, data suggestive of wakefullness in these preparations must be interpreted cautiously. If ability to learn is taken as evidence of arousal and sensory integrative capacity this would make a strong case for an interpretation of waking. Following brain stem transection habituation and conditioning trials were carried out when low-voltage fast activity had begun to appear in the "recovering" EEG records. We were successful in conditioning eye movements in the isolated portion of brain rostral to the transection using as the CS a previously neutral visual stimulus. The unconditioned stimulus was midline thalamic stimulation. Simple Pavlovian conditioning, discrimination, and generalization occurred during episode of low-voltage fast, but not high-voltage slow, EEG activity. We conclude that learning can occur in the portion of brain rostral to transection without participation of more caudal structures, and that this conditioning is indicative of a waking state in that the animal is capable of incorporating sensory stimuli and elaborating an appropriate motor response. (This work was supported by USPHS grants NB 02131 and MH 10320.)

THE RECONSTITUTION OF ANTIMYCIN A-INHIBITED SODIUM TRANSPORT BY PHOSPHOENOLPYRUVATE (PEP) IN THE PROXIMAL TUBULE OF RAT KIDNEY. R. Kinne and A.Z. Györy (C.J.Martin of NH & MRC of Australia). Max-Planck-Institut für Biophysik, Frankfurt/M., Germany.

Antimycin A, a specific inhibitor of the respiratory chain cytochrome b, inhibits isotonic sodium reabsorption measured with the split droplet method when applied intratubularly together with serum albumin (0.5%). Isotonic volume absorption (J_v) with 10⁻⁵M and 10⁻⁴M Antimycin A was 0.9 x 10⁻⁴mm³mm⁻²sec⁻¹ or 20% of normal. PEP (5 x 10⁻³M) given intratubularly together with albumin improved J_v maximally by 1.2 x 10⁻⁴mm³mm⁻²sec⁻¹ but only in the presence of 10⁻⁵M Antimycin A. Using 10⁻⁴M Antimycin A PEP is without effect. To find an explanation for this discrepancy, the effect of Antimycin A on the Na⁺-K⁺ ATPase of cell membranes isolated from rat kidney cortex was investigated. 10⁻⁴M Antimycin A inhibits the Na⁺-K⁺-ATPase totally whereas 10⁻⁵M inhibits only 50%. Thus, in the presence of 10⁻⁴M Antimycin A both the mitochondrial ATP production and the Na⁺-K⁺-ATPase are inhibited almost completely. Using 10⁻⁵M Antimycin A, ATP synthetized from exogenous PEP by pyruvatekinase can be used by the partly inhibited Na⁺-K⁺-ATPase for sodium transport. This demonstrates that:

- 1. Energy can be supplied from the outside of the cell for intracellular work;
- Sodium transport is coupled with Na+-K+-ATPase in renal proximal tubules.

THE PRESSURE-FLOW-RELATIONSHIP OF THE AUTOREGULATING KIDNEY VASCULATURE EVALUATED FROM BEAT BY BEAT IMPEDANCE LOOPS IN CONSCIOUS DOGS. <u>H.Kirchheim</u> and <u>R.Gross</u>, I.Inst.of Physiology, Univ. of Heidelberg, Germany

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In unanesthetized dogs abdominal aortic pressure was measured with an implanted miniature transducer(natural frequency: 20 kHz),left renal artery flow velocity by an electromagnetic flowmeter (- 3 dB at 100 Hz). The time lag caused by the flowmeter could be balanced by an appropriate distance between the transducers.Impedance loops were obtained recording flow versus pressure beat by beat on an oscilloscope. The impedance loops changed with arterial mean pressure; different pressure levels were induced either by bilateral common carotid occlusion or compression of the abdominal aorta, which did not change kidney mean flow. Electrical stimulation of the right cervical N. vagus resulted in prolonged diastolic decaies of single loops down to 25 mmHg blood pressure. The relation between flow (i) and pressure (P) followed the power function: $\underline{i} = \underline{a} \cdot P^n$. The exponent "n" decreased, the coefficient "a" increased with rising mean pressure. It is concluded, that a unique pressure-flow-relationship exsists for each level of arterial mean pressure; changes in mean blood pressure cause the kidney vessels to shift from one to another pressure-flow-relationship without altering kidney mean flow.

RELATIONS BETWEEN EVOKED DISCHARGES AND SPONTANEOUS ACTIVITY OF THE RENAL SYMPATHETIC NERVE IN ANAESTHETIZED CATS. F. Kirchner 1. Physiol. Inst. Univ., Heidelberg, Germany

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Electrical stimulation of spinal afferents or the posterior hypothalamus often elicits an evoked discharge in the sympathetic nerves. To elucidate the mechanism which is responsible for the occurrence of evoked discharges, we studied the correlation between evoked discharges in the renal sympathetic nerve and blood pressure, integrated sympathetic activity, and the timing in systole. The evoked discharges were elicited by single shocks of supramaximal intensity applied to sciatic nerve, dorsal root of TH10, the posterior hypothalamus, and the pressor area of the medulla oblongata. Changes in blood pressure and sympathetic activity were produced by pharmaca, hypoventilation and asphyxia. During periods of decreased spontaneous activity, evoked discharges on stimulation of the hypothalamus and the late supraspinal reflex discharge on spinal afferent nerve stimulation could not be obtained. On the other hand, regular observations during decreased sympathetic activity were evoked discharges on stimulation of the pressor area of the medulla oblongata and the early spinal reflex discharge on spinal afferent nerve stimulation. These results suggest: 1) The medullary sympathetic pressor area predominates over peripheral as well as hypothalamic influences. 2) The spinal reflex pathway is not influenced by the spontaneous medullary sympathetic activity.

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ON SOME PHYSIOLOGICAL CHARACTERISTICS OF IDENTIFIED CELLS IN THE CENTRAL NERVOUS SYSTEM OF LYMNAEA STAGNALIS. I.Kiss, J.Salánki and M.Véró. Biol.Res... Inst. of the Hungarian Academy of Sciences, Tihany, Hungary.

In the central nervous system of Lymnaea stagnalis giant neurons were

In the central nervous system of Lymnaea stagnalis giant neurons were identified on the basis of their physiological characteristics and chemical sensitivity. The neurons can be classified in three groups:(a) pacemaker neurons without synaptic input, (b) pacemaker neurons having also synaptic input and (c) neurons being silent at normal membrane potential level. 1)On the basis of the effect of ACh D and H cells can be distinguished among the pacemaker neurons. In most of the cases 5HT has excitatory effect on these cells, however in single cases inhibition was found. Among the D and H cells there are certain neurones which were stimulated by noradrenaline and dopamine, while pacemaker neurons belonging to the CILDA category show inhibition after dopamine application. 2) The reactions of driven cells and silent neurons were more complicated. It was found, that the ACh effect depends besides other factors - also on the resting potential level and on the actual type of activity.

904 EFFECT OF BIOLOGICALLY ACTIVE SUBSTANCES ON THE RESTING AND ACTION POTENTIALS IN GASTROPODA HEART. T.Kiss and Katalin S.-Rózsa. Biol. Res. Inst. of the Hungarian Academy of Sciences, Tihany, Hungary.

The resting and action potentials were registered from the isolated ventricle of Helix pomatia by microelectrodes. The duration, shape and the frequency of the action potentials were examined under the influence of biologically active substances. Acetylcholine (Ach) evoked inhibitory as well as excitatory effects depending on concentrations. Lower concentrations (10⁻¹⁰ - 10⁻⁸M) caused stimulation and higher concentrations (10⁻⁷ - 10⁻⁵M) caused inhibition. 10⁻¹⁴M eliminated the generation of action potentials. 5-hydroxytryptamine (5 HT) from 10⁻¹⁰M concentration increased the amplitude and duration of the action potentials and decreased the frequency.Adrenaline, noradrenaline and GABA caused an insignificant increase in frequency.Dopamine, tryptamine and tyramine had no effect on the generation of the action potentials. It is suggested that among the investigated substances Ach and 5 HT play a role in the regulation of the generation of action potentials in Gastropoda.

THE MECHANISM FOR ACETYLCHOLINE RELEASE FROM MOTOR NERVE ENDINGS. H. Kita and W. Van der Kloot, Dept. of Physiology, New York Univ. Sch. of Med., New York, New York, U.S.A.

Changes in the osmolarity of the Ringer are known to alter the properties of the ACh releasing mechanism of motor nerve endings. Increases in osmolarity markedly increase spontaneous release -- m.e.p.p. frequencies go up; but release from stimulated endings goes down -- e.p.p. amplitudes decrease. We have quantitatively tested the idea that the important variable is the ionic strength of the axoplasm, which alters the electrostatic interaction between surface charges on the ACh-containing vesicles and on the inner face of the axon membrane. Two lines of evidence support this idea. 1) Plots of log(m.e.p.p./ sec) or of log (e.p.p. amplitude) versus (osmolarity) 0.5 give straight lines. 2) Changes in m.e.p.p. frequency and in e.p.p. amplitude occur without substantial changes in activation energy; a characteristic of changes in reaction rates caused by shifts in ionic strength. We suggest that in the resting nerve the inner face of the membrane and the vesicles have surface charges of the same sign, so there is an electrostatic barrier opposing ACh release. When stimulated, the charge on the inner face of the nerve membrane changes polarity, perhaps by the binding of Ca++, so the vesicles are attracted to the membrane. The increase in the concentration of ions in the axoplasm may screen the charges on membrane and vesicles from one another and thereby decrease the ACh release

(Supported by grants from the USPHS.)

906 LEFT VENTRICULAR HEAT PRODUCTION AND OXYGEN CONSUMPTION IN THE INTACT DOG HEART. J. Kjekshus and O.D. Mjøs. Inst. Exper. Med. Res., Univ. of Oslo, Ullevaal Hosp., Oslo, Norway.

Since metabolic heat is removed from the middle of the myocardium mainly by coronary flow, heat might accumulate locally at a rate determined by the metabolism when the coronary flow is suddenly stopped. Myocardial heat production was therefore measured in thoracotomized dogs during 2-l0 sec occlusions of left coronary artery with thermistors inserted in the left ventricular wall. The initial rate of temperature rise, $\Delta T(^{\circ}C/\min)$, was used to calculate the metabolic heat production: $\dot{Q}=\Delta T\cdot s$, where \dot{Q} is in cal/min·g, and s = specific heat of the tissue. Following coronary occlusion, ΔT was linear for 2-5 sec before ventricular dilatation supervened. During control periods, \dot{Q} averaged 0.41 \pm 0.04. MVO2, determined simultaneously, was equivalent to 0.45 \pm 0.04 cal/min·g. A linear relationship between \dot{Q} and oxygen utilization was obtained over a wide range of metabolic rates induced by i.v. infusion of noradrenaline, angiotensin and isoprenaline, and by bleeding to 60 mm Hg. Results from all experiments fit the regression line 02-cons. (cal/min·g) = 0.93 \dot{Q} + 0.07, r = 0.97, n = 27.

CARBON DIOXIDE MEDIATED GLYCOLYSIS: A SIGNAL SYSTEM. G.A. Klassen and D.T. Zborowska-Sluis. McGill University Clinic, Royal Victoria Hospital, Montreal, Canada.

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Hydrogen ion inhibits erythrocyte glycolysis through its effect on phosphofructokinase. Keeping pH constant, and varying PCO_2 from 3.5 mm Hg to 35 mm Hg of incubated canine erythrocytes we observed reduction of lactate production at a constant glucose uptake. The accumulation of triose intermediates was associated with increased potassium uptake. This second control point, at a distal triose site, responds to CO_2 , and results in an alteration in the energy level of erythrocytes. Erythrocytes subjected to a changing pH and CO_2 environment will have altered energy levels, hence will have an altered oxygen and carbon dioxide transport capacity mediated through 2,3 DPG. Changes in erythrocyte gas transport capacity, when integrated by the circulation, may act as a metabolic signalling system between areas of active metabolism such as muscle, and areas of neural control such as the respiratory center, independent of gas tensions.

EFFECT OF HIGH BLOOD LACTATE CONCENTRATION ON MAXIMAL WORK PERFORMANCE. K.Klausen and H.G.Knuttgen. Lab. for the Theory of Gymnastics, University of Copenhagen.

908

The purpose of the present investigation was to investigate the influence of initial high arterial blood lactate concentration (LC) on maximal work performance capacity. Four young male subjects performed leg-work (Wmax) on a bicycleergometer. The work loads corresponded to an energy production which slightly exceeded the max. O_2 -uptake (V_{O_2} max) of the subjects. The Wmax was either preceded by a 30 min. rest period (I) or by a nonexhaustive period of arm work (arm ergometer) which gave an average LC of 10,2 mM/l at the onset of Wmax (II). Four experiments of each type were performed on each subject. Average values are presented in the table:

work type	Wmax kpm/min	Worktime min	V _{O2} max 1/min	peak lactate mM/1	△ lactate mM/1	
I	1792	5,00	3,729	12,9	11,8	
II	1792	4,49	3,746	15,3	5,1	

Peak lactate = 1-4 min. of exercise. ALactate = increase during exercise. Blood pH followed the changes in LC. It is concluded that a ten fold increase 100 LC before exercise only reduces the maximal work output slightly

VOLTAGE CLAMP ANALYSIS OF STRYCHNINE-INDUCED CONVULSIVE ACTIVITY IN APLYSIA NEURONS.
M.R. Klee, D.S. Faber and W.-D. Heiss, Neurosensory Lab., Dept. Physiol., SUNYAB, Buffalo,
N.Y., USA, and Max-Planck-Inst. Hirnforschung, Neurobiol. Abt., Frankfurt-M., Germany.

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In similarity with mammalian neurons, in 50% of identifiable neurons in the visceral ganglion of Aplysia strychnine in concentrations higher than those that block both inhibitory and excitatory synaptic potentials (0.5-2mM) causes convulsive, i.e. bursting activity, even though synaptic input is blocked. Also, in all cells there is an increase in spike duration and decreases in spike amplitude, afterhyperpolarization, and membrane potential, effects which are converted to long-lasting depolarizations if calcium concentration is reduced or cobalt chloride (30mM) is added. During voltage clamping of cells that start bursting, there is a shift of the threshold for the transient inward current to low-er voltage and —sometimes after a small increase with low concentrations— a reduction of the inward current. In contrast, outward current is always delayed with respect to voltage and reduced by as much as 70%. The time to peak of the inward current increases by about 20-50% and its duration and decay time are about 2-3 times longer. Adding cobalt further increases the described reductions; strychnine plus cobalt also blocks the slow potassium inactivation, the sag in late outward current during long depolarizations being reduced or abolished, with delayed development of a continuously growing outward current resulting. In cells showing the subthreshold potassium current, no change in its time course can be seen. Strychnine therefore seems to act as a convulsant by reducing both outward current and the inactivation of the early inward current.

910 ORIENTATION THROUGH OLFACTION IN FISHES. H.Kleerekoper. Inst. of Life Science, Texas A&M University, College Station, Texas 77843, U.S.A.

When sexually mature, the female of Ictalurus punctatus, a teleost fish, releases a pheromone which is strongly attractive to males of the species. A computer analysis of locomotor behavior, monitored by a matrix of photocells, demonstrated that, in a steep gradient, the orientation of the male towards the source of the pheromone is through chemotropotaxis. In a weak gradient, the stimulus alone is not sufficient to direct the resulting alarm movements. However, in the presence of a current, the specific olfactory stimulus releases positive rheotaxis which leads the animal to the source.

911 INFLUENCE OF NEONATAL SENSORY DEAFFERENTATION ON REGIONAL DEVELOPMENT OF BRAIN SEROTONIN AND NOREPINEPHRINE. A. Kling and J. Alverez. Dept. Psychiatry, Rutgers Med. Sch. New Brunswick, N.J. U.S.A.

Previous studies have shown that neonatal olfactory and visual deafferentation alters the time of puberty in the rat. The results of this study suggest that this effect may be related to differential changes in the rate of development of brain serotonin and norepinephrine. Of 540 rats, 1/3 were enculeated between the 5th and 7th post-natal day, 1/3 sustained olfactory stalk transsection and 1/3 served as unoperated controls. Equivalent numbers in each group were sacrificed at 20, 30, 60 and 90 days of age. Concentrations of serotonin and norepinephrine were determined for the amygdala, hypothalamus, cortex, caudate and hippocampus. After both procedures, significant increases in serotonin and decreases in norepinephrine were found in amygdala and hypothalamus, especially at 30 and 60 days of age.

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912 INHERITANCE OF AEROBIC WORK CAPACITY. Vassilis Klissouras. Ergophysiology Laboratory, Physiology and Physical Education Depts., McGill University, Montreal, Québec, Canada.

A simple additive model of heredity plus environment, based on intrapair differences observed in monozygous (mZ) and dizygous (DZ) twins, was used in this investigation to elucidate the heritability estimate (Hest):

Hest =
$$\frac{(\sigma^2_{DZ} - \sigma^2_{m}) - (\sigma^2_{MZ} - \sigma^2_{m})}{(\sigma^2_{DZ} - \sigma^2_{m})} \times 100$$

which signifies the proportion of the total variance of aerobic work capacity attributable to genetic variability. Twenty-five pairs of male twins (15 MZ and 10 DZ), whose ages ranged from 7 to 13 years and whose zygosity was determined on the basis of morphological traits and serological examinations, ran on a treadmill to exhaustion. The application of the above equation to data obtained, disclosed that the variability of maximal oxygen uptake is genetically determined by 93.4 per cent. It was concluded, that nature alone seems to account almost entirely for existing differences in aerobic work capacity among individuals, subject to similar environmental influences. (Supported by the Medical Research Council of Canada and the Québec Institute of Research in Education).

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FLOW DEPENDENT CHANGES IN THE LIGHT TRANSMISSION (LT) AND RHEOLOGY OF WHOLE HUMAN BLOOD.H.J.Klose and H.Schmid-Schönbein, Dept. of Physiol., Univ.Munich Munich, German Fed. Rep.

To correlate changes in the LT of flowing blood to its microrheological behaviour (as judged by viscometry and rheoscopy) whole human blood (Hct45%) was subjected to viscometric flow in a cone plate chamber (0-300sec) equipped with a photometric device (selenium barrier photo cell at 620mmu). Disaggregation of normal human blood at shear rates between 0 and 30sec is accompanied by decreases in LT, while cellalignment at shear rates above 30 up to 300sec leads to a progressive increase in LT. (Schmid-Schönbein et al. Fed.Proc.30,1971, in press). Non-aggregating RBC-samples (bovine whole blood and crenated cells in plasma) only exhibit high shear increase in LT (above 30sec). In heavily aggregated blood samples (myocardial infarction) the high shear increase in LT is missing. Conversely, RBC in 35% isotonic Dextran solution, aligned at very low shear rates, show increase in LT at 2sec . This differentiated optical behaviour explains contradictory data in the literature, where differences in species, Hct, shear rate and continuous phase have not been controlled. The results are not only pertinent for further rheological research, but are of practical interest for the application of photometric methods to the study of whole blood.

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EFFECT OF SELECTIVE WARMING THE EARS OF RABBITS ON THERMOREGULATORY RESPONSES. M.J. Kluger, R.R. Gonzalez and J.D. Hardy, John B. Pierce Foundation Laboratory, Department of Epidemiology and Public Health, Yale University, New Haven, Conn. U.S.A.

In New Zealand White rabbits, exposed at an ambient temperature of (8°C), selective heating of the ears to 30°C by thermal radiation led to a substantial decline in oxygen consumption generally associated with a drop in rectal temperature. The energy absorbed was measured to be 11 W/m^2 . As only the two ears were exposed to the radiation, skin temperatures in other areas (back, forelimb and hindlimb) did not change. After about 10 minutes, the initial decline of about 30% of excess oxygen consumption due to shivering corrected for heat input from thermal radiation. This decline was usually followed by an increase in metabolism and rectal temperature. These responses were generally greater during a second heating period some 30 minutes later. With cessation of heating, the oxygen consumption and rectal temperature increased – often to levels higher than the initial level at 8°C. Similar heating of the ears (40-42°C) at a higher ambient temperature (30°C) led to an increase in respiratory water loss. These results indicate that temperature sensors exist in the ears of these rabbits and provide an active peripheral thermoregulatory input.

FATTY ACID BIOSYNTHESIS IN THE PIKE (ESOX LUCIUS).J.H.F.M.Kluytmans.Laboratory of Chemical Animal Physiology, University of Utrecht, The Netherlands.

As very little is known about the pathways according to which fatty acids are formed by fishes, a system for fatty acid biosynthesis in vitro has been examined to study the formation of fatty acids by cell particles and cell-free supernatant from 1-14 C-acetate. Fatty acid synthesis is strong in 100.000 g supernatant from the liver, much lower in the kidney and low or absent in other tissues and organs that have been examined. The fatty acid synthetase in the particle-free supernatant is strongly stimulated by addition of citrate, bicarbonate and MgCl₂. For the cofactors ATP must be added and usually NADPH and CoA are also stimulating. Manganese ions are inhibitory in low concentrations, as are avidine and acyl-CoA esters. Fasting strongly decrease fatty acid synthesis; complete recovery is obtained about 48 h after refeeding. Incorporation of 1-14 C-acetate is predominant in 14:0 or 16:0 fatty acids, depending upon incubation conditions and is at its maximum at 25°C, decreasing at higher and lower temperatures. We are looking now for systems in mitochondria and microsomes, which can elongate the fatty acids formed 'de novo'.

914

THE INFLUENCE OF INHIBITORS ON THE ELECTRICAL PROPERTIES OF THE ISOLATED SALIVARY DUCT EPITHELIUM. H.Knauf, E.Frömter, B.Gebler. Max-Planck-Institut für Biophysik, Frankfurt/M., Germany.

The isolated salivary duct epithelium of the rabbit generates an electrical potential difference of up to 160 mV (lumen negative) when perfused with isotonic sodium sulfate solution. As in frog skin this transepithelial P.D. is a logarithmic function of luminal Na concentration and of interstitial K concentration. The addition of KCN (5x10-3M) and DNP (5x10-4M) to the bathing solution on the blood side of the duct causes the P.D. to fall nearly to zero and increases the specific electrical resistance of the duct wall. Despite the presence of inhibitors the luminal surface still behaves like a Na electrode and the contraluminal surface like a K electrode in accordance with USSING's model. The magnitude of the P.D. change for each tenfold change in Na concentration ("slope") falls, however, from 54 ± 3 mV before the addition of the inhibitor to 26 ± 5 mV afterwards. Similar changes in electrical properties occur when nonmetabolic inhibition is induced with quabain (5x10-6M) or by removal of K. Considering an equivalent circuit with two batteries in series representing luminal and basal cell sides and a small paracellular shunt conductance the findings can be explained by an increase of the internal resistance of either battery. Hence one need not conclude that the inhibitors affect the Na conductance of the luminal membrane. An increasing resistance of the basal cell membrane, where the Na-K-pump is thought to be located, would lead to identical results.

POUTES OF PERMEATION OF SULFHYDRYL REAGENTS INTO THE HUMAN RED BLOOD CELL MEMBRANE. P. Knauf and A. Rothstein. Yale Sch. of Med., New Haven, Conn. and Univ. of Rochester Sch. of Medicine and Dentistry, Rochester, New York, U.S.A.

The amino-reactive agent, 4-acetamido-4'-isothiocyano-stilbene-2, 2'-disulfonic acid (SITS) inhibits the penetration of the sulfhydryl reagent, parachloromercuriphenylsulfonic acid (PCMBS), into the interior of the membrane by more than 50%. This reduction in uptake, however, does not decrease or delay the potassium loss caused by PCMBS binding to sulfhydryl sites within the membrane. SITS also has no effect on the inhibition of active transport (measured by ouabain-sensitive Na efflux) produced by the binding of PCMBS to another class of sulfhydryl groups within the membrane. These results suggest that two distinct pathways for PCMBS entry exist, one of which is blocked by SITS and the other of which leads to the intramembrane sulfhydryl sites which are involved in both active and passive cation transport. This hypothesis is supported by the observation that chloride and sulfate have different effects on the SITS-sensitive and SITS-insensitive PCMBS uptake. Parachloromercuribenzoate (PCMB) penetrates the membrane more than three times as fast as PCMBS, and its uptake is not inhibited by SITS. PCMB also increases K⁺ loss, but to a far smaller extent than PCMBS. The rapid uptake of PCMB is presumably due to its greater lipid solubility, but entry through this pathway does not enable it to reach the cation controlling sulfhydryl sites. (Supported by AEC contract W-7401-ENG-49 and U.S. Public health Services Training Grant # 5 Tl GM 1088.)

918 EFFECT OF IONIZING RADIATION ON THE PSYCHIC PERFORMANCE OF RATS. Bertha Knoll. Dept.of Pharmacology, Semmelweis Medical School, Budapest, Hungary.

Radiosensitivity of the CNS is a field of severe contradictions. Data referring to both extreme sensitivity and extreme resistance have been published. We have applied a special method for the investigation of the psychic performance of irradiated rats. Rats placed onto a metal plate of 70°C under a glass cylinder jump onto the upper rim of the cylinder / unconditioned escape. After a 20 day training, an extremely firm conditioned reflex can be detected in every animal. In about 50% of the population, a peculiar "cylinder seeking" behaviour develops. These animals look for and are capable of finding the glass cylinder in a completely unknown environment. First stage of performance: Adult rats exposed to irradiation of 200-400 r x-ray to the whole body did not differ in their psychic performances from the controls. Rats irradiated as newborns and trained when they became adult reached only the first stage of performance, but none of them became "cylinder seeker". The very same animals lost their fertilizing ability, referring to an essential role of endocrine injury in the observed phenomena.

CELLULINE-A: AN ENDOGENOUS ORGANIC CALCIUM COMPLEX WITH HIGHLY SPECIFIC BIOLOGICAL ACTIVITY. J.Knoll. Dept.of Pharmacology, Semmelweis Medical School, Budapest, Hungary.

919

Stillstand of an isolated frog heart in Ringer' solution containing 27 mM KCl, 2x10⁻⁶ tetrodotoxin /TTX/ and 2.5x10⁻⁷ LB 46 cannot be antagonized with any known cardiotonic compound, but within a couple of hours, activity spontaneously restores. A substance, celluline, stemming from the auricle is responsible for adaption. Washing the inner surface of the frog skin with a solution of 112 mM NaCl + 27 mM KCl results in the appearance of celluline-A, which brings frog or cat heart preparations into action when stillstand was exerted by washouts with physiological solutions containing 27 mM KCl, 2x10⁻⁶TTX and 2.5x10⁻⁷LB 46. Celluline-A was purified by repeated gel filtration using Bio Gel P-2. The biologically active material is an organic Ca complex. Ca removal by oxalate splits the complex, and by the aid of Amberlit IRC-50, the ligands were separated and identified. Mass spectrometry and UV analysis proved that one of the organic ligands of celluline-A is p-tyramin and a second ligand contains pyridine. Data argue in favour that celluline operates as a "transformer substance" playing a crucial role in the chain of events which allow the heart cell membrane to be transformed from the resting state into excitation.

DISTRIBUTION OF FILTRATION IN SUPERFICIAL AND DEEP NEPHRONS IN THE DOG. F.G. Knox, E.G. Schneider, and R.E. Lynch. Dept. Physiology, Univ. of Missouri, Columbia, Mo., USA.

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The distribution of filtration in the superficial, intermediate and juxtamedullary nephrons of the dog was estimated from micropuncture, clearance, and histologic methods. The average superficial nephron filtration rate of 134 tubules of 33 hydropenic dogs was 59.2 \pm SE 3.4 nl/min and the glomerular filtration rate of the micropunctured kidney was 27.0 \pm SE 1.5 ml/min. There were 348,000 \pm SE 17,000 glomeruli per kidney as determined from an india ink injection method. The diameters of juxtamedullary and intermediate glomeruli from histologic sections were 7.5 and 4.5% larger than the superficial glomeruli respectively. The superficial, intermediate, and juxtamedullary zones from which these diameters were taken contained 29.7 \pm SE 1.4%, 37.6 \pm SE 2.9% and 32.6 \pm SE 2.4% of the total glomeruli respectively. From these values, the assumption that filtration is proportional to the cube of the diameter, and a calculation to account for differences in filtration pressure and membrane permeability, filtration rates of 77 nl/min and 84 nl/min were estimated for intermediate and juxtamedullary nephrons respectively. It is concluded that the superficial nephron filtration rate is significantly less than that of the deep nephrons in the dog.

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THE EFFECT OF DYNAMIC MUSCLE WORK BY CONCENTRIC AND ECCENTRIC CONTRACTIONS ON HUMAN SKELETAL MUSCLE METABOLITES. H.G.Knuttgen and F.Bonde Petersen. Institute of Physiology, Gymnastik och Idrottshögskolan, Stockholm, Sweden and Institute for the Theory of Gymnastics, University of Copenhagen, Denmark.

It has been suggested that skeletal muscle possibly absorbs mechanical energy during eccentric exercise and transforms this energy into chemical energy. If this is so in human muscles has never been proved. In the present experiment concentric bicycle exercise was performed on a Krogh bicycle ergometer and eccentric exercise on an ergometer described by Bonde Petersen (1969). An eccentric work load of 230 W was used and compared to two concentric work loads producing either the same muscle tension (230 W) or the same oxygen consumption (70 W). In addition an eccentric load of 70 W was used. The work periods were 4 min, and 7 subjects participated. By means of needle biopsies ATP, CP, Lactate, Glucose and Glycogen were analyzed in the vastus lateralis muscle, before, just after and 6 min after exercise with either of the four conditions mentioned. No sparing effect of eccentric work was seen upon the break down of the chemical substances analyzed.

922 MUSCLE METABOLISM IN SHORT-TERM EXERCISE AT ALTITUDE. H.G. Knuttgen and B. Saltin. Fysiologiska institutionen, Gymnastik- och idrottshögskolan, Stockholm, Sweden.

Oxygen consumption (Vo₂) and muscle metabolism were studied in human subjects performing 4 min exercise at a wide range of work intensities on a bicycle ergometer at sea-level and at 4,000 m simulated altitude (decompression chamber). Vo₂ was determined (Douglas bag/Haldane) throughout work and recovery. Muscle biopsies (m. quad. fem.) were taken before, immediately after, and 6 min after exercise. Under both work conditions, a lowering of high-energy phosphate compounds (ATP, CP) was observed at all work intensities. At approximately 50-60% aerobic capacity, increases in both muscle and blood lactate concentrations were observed, with concentrations proportional to work intensity. At these same work intensities, high-energy phosphate concentrations became markedly reduced in inverse proportion to work load. It would appear that, during the first minutes of exercise, there is a critical relative work load above which certain anaerobic phases of metabolism are brought into increasing degrees of participation. Parameters such as oxygen deficit, oxygen debt, as well as muscle metabolite concentration, show more consistent relationships when compared to relative work load (Vo2 in % of aerobic capacity under the specific environmental condition) than to absolute work load.

923 MODE OF ACTION OF HYPOTHALAMIC RELEASING FACTORS IN THE RELEASE OF TROPHIC HORMONES FROM THE PITUITARY GLAND. K.Kochman and E.Dománski. Inst.of Animal Physiology, Polish Academy of Sciences, Jablonna n. Warsaw, Poland.

In order to obtain some information on the mode of action of hypothalamic releasing factors in the release of trophic hormones from the pituitary gland, the effect of purified luteinizing releasing factor (LHRF) on the solubilization of the pituitary hormonal granules, and on the activity of pituitary phosphatase was investigated. Moreover, the effect of cyclic nucleotide 3'-5'monophosphate (c-AMP) on the release of luteinizing hormone (LH) from the pituitary gland was investigated. Results: (1) on the basis of the results of LHRF action on the anterior pituitary homogenates and on the isolated and purified anterior pituitary granules, containing LH, it is suggested that this substance in the process of LH release from the pituitary gland displays its action on the cells and on their enzymatic system (phosphatases or other enzymes), rather than directly on the secretory granules. (2) A negative effect of c-AMP on the release of LH from the pituitary gland, obtained in vivo experiments, seem to indicate that this substance is not able to simulate action of LHRF in the environment very near to physiological conditions.

924 CENTRAL TRANSMISSION OF PULMONARY INFLATION AND DEFLATION REFLEXES. +
H.P.Koepchen, D.Klüßendorf, M.Bilan, N.Sapunarow a. D.Sommer
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The question is, if the known exitation of different receptors at the various states of lung inflation is accompanied by a similarly complex reaction of brainstem respiratory neurons. Previous authors have described some partly contradictory findings, especially on expiratory neurons (e.n.).

Microelectrode studies in the lower brainstem of anethetized dogs in the center of the juxtabranchial inspiratory and expiratory populations show that the discharge frequency of these rather uniformly reacting neurons is a continous function of lung distension: Inspiratory neurons (i.n.) are activated by deflation and inhibited by inflation until total silence at moderate inflation. E.n. react biphasically: Deflation leads to inhibition, inflation to activation until a"critical" lung volume is reached. Thereafter inhibition takes place again. The "critical" volume diminishes with increasing rate of distension. Thus during deflation and moderate inflation i.n. and e.n. are influenced in opposite direction by lung volume changes, whereas during strong inflation both are inhibited. This latter effect is interpreted as a more general inhibition of reticular activity.

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THE PROBABILISTIC NEURON ENSEMBLES FUNCTIONAL ORGANIZATION OF THE HIGHEST PARTS OF THE BRAIN. A.B. Kogan. Rostov State University, USSR. 925

The conception of the probablistic-statistical organization of the highest brain parts in the vertebrate animals was suggested and proved by the neurophysiological experiments. The functional units was shown by the neurophysiological experiments. The functional units was shown to be not single neurons but their ensembles. The latter arise at each afferent stimulus as groups of neurons which participate in responses in a probablistic way. Each ensemble has the excited centre and the inhibited fringe. The spacial, temporal and informational parametrs of such ensembles form patterns manifesting the character of the stimulus and functional state of the brain. Narcosis, for example, enlarges the ensemble sizes and makes their boundaries blurred, natural sleep increases the correlation of evoked impulse currents of neurons at vast regions of the cortex. The evolution of the visual analyzer from from the ons of the cortex. The evolution of the visual analyzer from frog to cat shows the decrease of ensemble sizes and the increase of their number on the projection field surface unit, raising the permitting ability of the vision.

ACTIVE CENTER OF TRANSPORT ATPASE. I.S.Koh. Dept. of Physiology, School of Medicine. Kyung Hee University, Seoul, Korea.

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The aim of these experiments were to summarize the evidence that justified the active center of transport ATPase: (1) the action of the pump is associated with the ouabain - sensitive ATPase activity that depended on the presence of sodium plus potassium ions; (2) this enzyme is reversible in NaF poisoned red cells; (3) the cysteine which prevented the loss of potassium from the cells poisoned by heavy metals; (4) the results suggest that sulfhydryl group does act as an active center of transport ATPase.....

SELECTIVE INHIBITION OF Ca CONDUCTIVITY OF MAMMALIAN CARDIAC FIBRE MEMBRA-NES BY Ca-ANTAGONISTIC COMPOUNDS (VERAPAMIL, D 600). M.Kohlhardt, B.Bauer, H.Krause and A.Fleckenstein. Physiological Institute, University of Frei-

burg, Germany.

The transmembrane Na and Ca inward currents were measured independently on ventricular trabeculae of cats using the voltage clamp technique (1,2). According to earlier studies on papillary muscles, verapamil and D 600 (a methoxy-derivative of verapamil) can abolish the Ca-dependent contractile responses completely whilst the Na-dependent action potentials persist (3, 4). The present investigation has clarified the mechanism of action since verapamil (2 mg/l) or D 600 (0.5 mg/l) blocks the transmembrane Ca inward current completely without reducing the transient Na current. The Ca inward current, as well as contractility, is restored by an increase in extracellu-lar Ca even in the presence of relatively high doses of Ca-antagonistic drugs.

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928 SODIUM PUMP IN CAT PYRAMIDAL TRACT CELLS. H. Koike, N. Mano, Y. Okada and T. Oshima.

Dept. Physiology, Toho Univ. Sch. Med. and Dept. Neurophysiology, Inst. Brain Res., Sch. Med., Univ. Tokyo, Tokyo, Japan.

The technique of an electrophoretic ion injection into cells is most valuable in the studies on mammalian neurones since it has usually been impossible to control their ionic environment in the extracellular space. In the present experiment, sodium ions were injected into cat pyramidal tract (PT) cells electrophoretically through an intracellular NaCl- or Na glutamate-filled microelectrode. Following an injection there were characteristic changes in the resting and spike potentials, the after-potential, and the inhibitory postsynaptic potential, all of which recovered within 5 minutes. As in cat spinal motoneurones, the time courses of recovery in the rising and falling slopes of the spike were exponential and parallel with each other, indicating a reciprocal change in the intracellular sodium and potassium concentrations under the operation of the sodium pump in extruding actively excess sodium ions. From the exponential recovery curves, the rate constant of active sodium extrusion was estimated as about 60 per hour for large PT cells. In addition, that the sodium pump in PT cells was at least partly electrogenic was suggested from the following two observations. First, the resting membrane was hyperpolarized by sodium injection to the degree which depended on the amount of sodiuminjecting current. Secondly, high-frequency activation of PT cells developed a posttetanic hyperpolarization, and its late component was not dependent on the increased membrane permeability to potassium ions.

WHICH AREAS IN THE BRAINSTEM ARE INVOLVED IN SOMATO-SYMPATHETIC REFLEX?

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Major components of somato-symp.reflex (late reflex and "silent period")

Major components of somato-symp.reflex (late reflex and "silent period") are shown to be dependent on intact medulla obl.. It was questioned if there are any specific areas in this region which are responsible for the transmission of these reflex components. In chloralose anaesthetized cats, symp. reflexes were recorded from L₁₋₂ white rami and renal n. following stimulation of fore and hind leg afferents. Bilateral lesions of inspiratory or expiratory neuron groups or baroreceptor afferent relay neurons in tract.sol.nucl. did not abolish late symp. reflex and/or "silent period" though phrenic discharge or baroreceptor reflex disappeared as well as phrenic or pulse synchroneous waves in symp. activity. Small bilateral lesions in various parts of the brainstem did also not affect symp.reflex. Only large bilateral lesions which caused a drop in blood pressure and a loss of spontaneous symp. activity abolished these reflexes. However background activity and reflexes returned to control level after 30-60 min if blood pressure was maintained artificially at levels over 100 mmHg. It was concluded that late symp. reflex and "silent period" are normally integrated in greater parts of unspecific reticular form.. After greater lesions this integration is out of function but if blood flow is kept normally other parts can take over. (Supported by USPH grant NS-847).

930 SLOW ELECTRICAL ACTIVITY IN THE MEDULLA OBLONGATA OF FISHES. N.N.Kokina, V.A.Safonov, T.S.Sterlina. Dept.of Animal Physiology, State Univ., Moscow, USSR.

Slow spontaneous electrical activity of surviving fish brain structures/Carp,Crucian Carp,Goldfish/ was studied. Given the suitable conditions, tissue cultures and explants/0,3-3mm/ in a month in vitro demonstrated the presence of all cell types, characteristic for nervous tissue in vivo.Electrical activity of the cultivated fragments of medulla respiratory structures was compared with the activity of the same structures from a whole isolated /according to Adrian/ brain and from non-extir pated fish brain. The microelectrode technique was used. Recording pattern show two forms of electrical discharges: spike bursts of large neurons /30mc. and more/and slow typical waves/from 0,1sec. and more duration/apparently produced by smaller cells/10-15mc./. Isolated brain retain slow waves in 90% cases, but spike barrage only in 30%. Cultivated fragments are active in 30% cases. Their size and cellular compound determine the form of electrical activity and its existence. To the authores way of thinking, siow electrical waves may control the spike bursts of respiratory center's neurons.

1sec. 20 mcv.

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SYMPATHETIC ACTIVITY DURING AND AFTER SPINAL CORD TRANSECTIONS.

M. Kollai, A.G.B. Kovách and L. Fedina. Exper. Res. Dept. Semmelweis Med. Univ. Budapest, Hungary.

Activity of postganglionic sympathetic nerves of heart and kidney was continuously recorded during and after transection of the spinal cord first at the Th5-6 and subsequently at the C1-2 level. For stimulation we used the Th2 and L2 spinal nerves as segemental somatic afferents. During the spinal cord transection the activity of both nerves increased; after having completed the transection the activity considerably decreased as compared to the pre-transection level, the former pulse synchronous groups disappeared but there still existed a reduced irregular activity in contrary to data reported previously; the segmental somatosympathetic reflex response could be elicited immediately after the transections although with smaller amplitude; the reflex response was followed by an inhibitory phase of the spontaneous background activity; the sympathetic efferent activity was also inhibited by elevating the blood pressure by 10 ug/kg of Noradrenaline.

CENTRAL EFFECTS OF NORADRENALINE /NAd/ AND GAMMA-AMINOBUTYRIC ACID /GABA/ON THERMOREGULATION IN THE NEW-BORNS; Ibolya Komáromi. Dept. of Pathophysiology, Univ. Med. Sch. Pécs, Hungary.

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5 µg NAd was injected into the lateral cerebral ventricle of unanaesthetized rabbits aged 1 day to 15 days. In the new-born rabbits
oxygen consumption increased but the effect became successively smaller
with age, practically disappearing on the 15th day of age. The most
marked response was obtained in animals kept at a neutral environmental
temperature. At lower temperatures the increase in basal oxygen uptake
was associated with a smaller response to NAd.

was associated with a smaller response to MAG.

GABA in a dose of 10 µg augmented oxygen uptake and body temperature in the new-born rabbit and guinea-pig. The response depended on the environmental temperature, the greatest increase occured at neutral temperature. Unlike NAd however there is no decline in sensitivity with age between 1 and 12 days.

According to Kordoveni Moore and Singap, the new-born rat does not

According to Komáromi, Moore and Sinanan the new-born rat does not respond to GABA. So we have to take into consideration not only deve-lopmental, but species differences in the response to chemical transmitters.

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THE COMBINED EFFECT OF SECRETIN AND CHOLECYSTOKININ ON THE VOLUME AND ALKALINE CONTENT OF PANCREATIC JUICE. S.J. Konturek, T. Radecki, E. Mikoś, P. Thor and J. Kaulbersz, delivered by J. Kaulbersz.
Inst. of Physiology, Med. Academy, Cracow, Poland.

Pancreatic secretory studies were carried out on 9 concious cats provided with chronic gastric and pancreatic fistulas performed by modification of the method of Herrera et al. Pancreatic volume flow and alkaline output were determined in response to the combined action of secretin introduced intravenously or secretin released by acidification of the intestine and CCK infused intravenously or released from the intestinal mucosa by phenylalanine. Maximal response to exogenous secretin was obtained at the dose of 4 units per kg/hr and was almost identical with that at the dose of 0,5 units per kg/hr combined with graded doses of CCK. Pancreatic secretion produced by endogenous secretin was highest at the rate of 2 mEq/hr of acid although it was 15% lower than the maximal response to exogenous secretin. When graded doses of CCK were added, similar response was achieved at the rate of 0,5 mEq/hr of acid. Endogenous CCK, like exogenous, alone did not produce a measurable increase in pancreatic secretion, it increased only pancreatic volume flow and alkaline output when a background dose of exogenous or endogenous secretin was used. A synergism exists also in this regard between secretin and CCK.

934 LOCALIZATION OF SECRETIN AND CHOLECYSTOKININ RELEASE IN SMALL INTESTINE OF THE DOG.
S. J. Konturek, J. Tasler and W. Obtulowicz. Inst. of Physiology, Medical Academy, Krakow, Poland.

Several groups of dogs with a Pavlov pouch (PP), gastric fistula (GF), pancreatic fistula and Thiry loops fashioned from various levels of the small intestine were used in the study. Endogenous secretin and cholecystokinin (CCK) were released by perfusion of the intestinal loops with 0.1 N HCl and 0.15 M L-phenylalanine, respectively. The GF was open throughout the experiments to drain gastric juice to the exterior. Pancreatic volume, bicarbonate and protein outputs as well as the half maximal gastric acid response of the PP to pentagastrin were examined during irrigation of intestinal loops with varying amounts of test solutions and compared to those elicited by various intravenous doses of secretin and CCK. Acid perfusion of the duodenum only resulted in a strong inhibition of the PP response whereas stimulation of pancreatic volume and bicarbonate output occurred during acid irrigation of the duodenum and upper jejunum but not distal jejunum and ileum. Perfusion with L-phenylalanine decreased the PP acid response and stimulated pancreatic protein output from both duodenum and jejunum but not the ileum. The amounts of releasable secretin and CCK in the upper part of the small intestine were related to the rate of perfusion and the length of intestine perfused. This study indicates that the mechanism for the release of both secretin and CCK in widely distributed in the duodenum and upper part of the small intestine.

935 ON THE CALCIUM-BINDING SITES OF FROG MUSCLE TREATED BY PHOSPHOLIPASE-C. L.Kónya, A.Csabai. Dept.of Physiology, Univ.Med.Sch.Debrecen, Hungary.

Phospholipase-c /PL-C/ modifies the structure of membranes by splitting polar groups of their phospholipids. Changes in the membrane potential, ionic composition and extracellular space of frog skeletal muscle treated by PL-C indicate a significant change in the permeability properties of the surface membrane. 45-calcium equilibrates in the presence of 5 mM ATP with about 3 mM muscle calcium. Without ATP muscle activity is less than the half of that even after 24 hours incubation. Desaturation curve of 45-calcium in both cases is biphasic. The fast component has a half life of about 37 minutes and amounts 18±5,5% of the total activity in the presence and 85±2,8% in the absence of ATP. The half life of the slow component is 178±24 minutes and amounts 82±5,5% in the presence and 566±150 minutes and 15±2,8% in the absence of ATP. In the presence of ATP most part of calcium is supposed to be accumulated in the sarcoplasmic reticulum and can be regarded specially bound. This part is sensitive to the absence of ATP, or to AGTA and PCMB.

936 VOLTAGE-CLAMP OF CARDIAC MUSCLE: A THEORETICAL ANALYSIS. J.M. Kootsey, E.A. Johnson. Dept. of Physiology and Pharmacology, Duke University, Durham, N.C. 27706, USA.

The theory of feedback systems has been applied to voltage-clamp preparations of cardiac muscle, representing the muscle fiber by a multi-section lumped-element model in a digital computer. Stability of the closed loop system requires that response time of the control amplifier (and thus of the entire clamp) must be long in comparison with the time required for voltage to propagate the length of the muscle being clamped. Voltage-clamp preparations in the literature do not meet this requirement, yet they are stable. It is suggested that a more realistic model, based on what is known about the structure of cardiac muscle preparations, must be used to interpret the voltage-clamp data.

This work is supported by Public Health Services Grants HE12157 and HE43004

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EFFECT OF ACTH AND ADRENOCORTICAL HORMONES ON BRAINSTEM MULTIPLE UNIT ACTIVITY (MUA) DURING HABITUATION AND SLEEP-WAKEFULNESS CYCLE IN THE CAT.

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In chronically implanted freely moving cats it was found that: 1. The MUA levels gradually decreased in the mesencephalic reticular formation, medial forebrain bundle at the anterior lateral hypothalamic level, preoptic area, fornix and the non-specific thalamic nuclei during habituation to a novel environment in the course of consecutive sessions. 2. ACTH, cortisol, corticosterone and cortisone resulted in a marked, general decrease in MUA both in habituated and non-habituated normal and adrenalectomized animals. 3. ACTH and cortisol reduced, while corticosterone and cortisone increased both the number and duration of paradoxical sleep cycles on the day of injection. These findings may represent an electrical correlate of the behavioral phenomena known to be induced by ACTH and corticoids administration.

HEPATIC AND RENAL THRESHOLD OF GLUCOSE UPTAKE AND RELEASE IN NORMAL AND DIABETIC RATS. R.Korec. Dept. of Pathophysiology and experimental Pathology, Medical Faculty of Univ.P.J.Safárik, Košice, Czechoslovakia.

The correlation between hepatic threshold of glucose uptake and renal threshold of glucose release was studied in normal, mildly and moderately alloxan disbetic adult fasting rets. In pentobarbital anesthesia, the left hepatic vein, portal vein, abdominal aorta, vens cava inferior and urinary bladder were catheterized and blood and urine samples were taken at 10 minutes intervals before and after duodenal injection or continual intravenous infusion of glucose into rats without or after alpha, or combined alpha and beta adrenergic blockade.

It was found that in both normal and disbetic rats the hepatic threshold.

It was found that in both normal and disbetic rats the hepatic threshold of glucose uptake is lower than the renal threshold at which glycosuria appears. In mildly or moderately diabetic rats with fasting glycemia up to 300 mg/100 ml, the liver takes up glucose also without exogenous insulin, however, both hepatic and renal threshold are significantly elevated. The hepatic threshold can be depressed by intraportal infusion of insulin.

These findings are discussed from the standpoint of their significance in adaptation and compensation in the healtly and diabetic condition.

QUANTITATIVE ASSESSMENT OF THE INTRINSIC MYOCARDIAL CONTRACTILITY IN SMALL LABORATORY ANIMALS. B.Korecky, G. Taichman, Department of Physiology, Univ. of Ottawa, Canada.

A considerable amount of cardiovascular research has been done on small laboratory animals, however their intrinsic myocardial mechanics have not been fully investigated. Utilizing laboratory rats, two methods of quantitatively determining myocardial contractility were achieved by calculating the theoretical maximum velocity of shortening in muscle lengths/sec. (Vmax). The in vitro method has utilized isolated papillary muscles where force-velocity curves were generated by a series of afterloaded isotonic twitches. Plots of initial shortening velocities versus the load lifted yielded curves whose velocity intercept expressed Vmax. The in vivo method has utilized closed chest anesthetized rats. Left intraventricular pressures were measured by a high-fidelity catheter recording system. Force-velocity curves were constructed by plotting the ratio of the pressure's derivative (dP/dt) to the product of the pressure (P) and the coefficient of series elasticity against the corresponding P. Extrapolation to zero P allowed estimation of the Vmax. The Vmax was relatively insensitive to changes in preload or afterload, while inotropic alterations changed Vmax. Using both methods in an experimental situation the hypophysectomized (Hx) rat displayed a depressed Vmax, while subsequent thyroxine (T4) treatment normalized this index. Although the absolute values of Vmax obtained by the two methods differed, the relative alterations seen after Hx and T4 were the same. Supported by the MRC of Canada and the Ontario Heart Foundation.

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940 CENTRAL RESETTING OF ARTERIAL BARORECEPTOR REFLEX. P. I. Korner and J. Shaw. Department of Medicine, University of Sydney, Sydney, Australia.

The arterial blood pressure was raised or lowered in unanaesthetized rabbits by inflating balloons around the aorta and inferior vena cava. The reflex effects on heart period were determined in sham-operated, thalamic and pontine preparations; each with (i) both autonomic effectors intact, (ii) after vagal block, and (iii) after sympathetic block. There was little difference in set point and gain for the baroreceptor reflex between the three neurological preparations whilst the animals were breathing air. During arterial hypoxia (pO₂ 30 mm Hg) there were marked changes in the 'baroreceptor function curves'. Immediately after the start of hypoxia the heart rate was unresponsive to changes in arterial pressure in thalamic and sham animals, but not in pontine. Later there was elevation (20 mm Hg) in 'set point' in pontine animals, suggesting that autonomic motoneurons were less than normally responsive. In thalamic and sham rabbits there was lowering in 'set point' (15-25 mm Hg), suggesting enhancement of autonomic motoneuron excitability.

941 AGE PECULIARITIES OF THERMOGENESIS AND DEVELOPMENT OF MITOCHONDRIAL MECHANISMS OF TISSUE RESPIRATION. I.A.Kornienko, G.M.Maslova, I.I.Gohblit. Inst. of Age Physiology. Acad.of Pedagogical Sciences, Moscow, USSR.

At the end of the 3rd week of life, an increase in the activity of mechanisms of chemical thermoregulation can be observed in rats. The value of heat production on the unit of weight is maximal during this age period. This can be explained by activation of mechanisms of non-shivering thermogenesis and is not connected with the increase of oxidation capacity of skeletal muscles. The content of citochrome "a"in skeletal muscles of 4 and 20 day rats is 17% from the overall content of citochrome"a"in the body, while in the tissue of inner organs, mainly in the liver, it increases from 46.6% in 4 day rats till 73.5% in 20 day rats. Development of shivering thermogenesis in older animals is related to the considerable increase in cytochrome"a"in skeletal muscles to 68.7% and, with the decrease in tissue of inner organs. The content of cytochrome"a"in brown fat is 35.6% in 4 day rats and in 20 day rats it decreases to 8.7%. We have not found any decrease of metabolism reaction on injection of norepinephrine 6 days after extraction of interscapular brown fat in 20 day rats. Simultaneously, these animals showed an accelerated development of oxidation in skeletal muscles (considering the content of cytochrome"a") and activisation of mechanisms of shivering thermogenesis.

COMPARISON OF THE REFLEX CARDIOVASCULAR RESPONSES TO DIFFERENT TYPES OF FEED BACK CONTROLLED CAROTID SINUS NERVE STIMULATION. J. Korsukewitz, K. H. Dittberner, J. Wagner and E. Zerbst. Physiologisches Institut, Freie Universität, Berlin, Germany.

In anaesthetized dogs (chloralose) the carotid sinus nerves(CSN) were stimulated (1): by equidistant impulses (30/s),(2): by impulse groups from a blood pressure feed back controlled electr.baroreceptor analog, (3): by impulse groups from a heart rate feed back controlled receptor analog and (4): by heart rate triggered impulse trains. (Frequency in the train was $65/\sec$, train duration in (3) & (4) was 150 msec. The impulse groups in (3)&(4) exhibited similar characteristics as those of natural baroreceptors: the mean impulse rate depends on blood pressure and or heart rate, each group is instituted by a high momentary frequency. The comparison of responses to CSN-stimulation according methods(1)-(4) showed the following results: The depressor effect on systemic blood pressure was most effective with method(2) and less effective with (3),(1)&(4). The suppression of heart rate was most effective with method (3) and less effective in the sequence(4),(1) & (2). This was valid for short term stimulation as well as for long term stimulation. CSN-stimulation by impulse groups with high initial frequency thus is most effective in experimental (baropacing) cardiovascular control.

REGULATORY FUNCTION OF THE INTRACARDIAC NERVOUS SYSTEM. G.I.Kositzky. Dept. of Physiology, Second Medical Institute, Moscow, USSR.

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The morphological study of dog's heart II-141 days following homotrans-plantation and degeneration of nerve fibres of extracardiac origin has shown a great number of non-degenerated efferent, afferent and intermediate neurons. They compose the intramural nervous system organised according to the reflex principle. Free endings of the dendrites of afferent neurons form the receptors of distension (strecht receptors) of the myocardium and coronary vessels. The intracardiac efferent neurons represent the final common path for the impulses of intracardiac and extracardiac origin. At strong impulsation, the cardiac activity is inhibited. The effect is accompanied by the release of acetylcholine and is blocked by atropine. At wear impulsation, the cardiac activity is enhanced. The effect is accompanied by the release of catecholamines and is blocked by adrenolytics. Hence, the intracardiac ganglia contain also adrenergic efferent neurons, which are second source of adrenergic cardiac innervation - a part of the intramural reflex mechanism. They are probably excited at the decrease of venous inflow. The increase in myocardial contractions improves the emptying of the heart, maintaining the blood filling of arterial system and facilitating the venous inflow.

THE MONOSYNAPTIC ACTION OF PROPRIOSPINAL PATHWAYS UPON MOTONEURONES. P.G.Kostyuk, D.A.Vasilenko. Bogomoletz Inst. of Physiology, Kiev, USSR.

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The lateral basilar parts of the dorsal horn contain interneurones that send axons into the dorsolateral funiculus. These axons pass several segments and ramify in the gray matter. A selective direct stimulation of such axons was performed in cat lumbar cord 2 weeks after ipsilateral hemisection in lower thorasic region resulting in degeneration of long descending pathways in the same funiculus. The volley in propriospinal axons (conduction velocity about 40 m/sec) evokes EPSPs in the majority of flexor motoneurones and IPSPs and EPSPs in extensor motoneurones of the neighboring segments, as it was shown by recording of ventral root monosynaptic test discharges and intracellular recording from single motoneurones. Latency measurements indicate monosynaptic nature of at least part of both EPSPs and IPSPs. Propriospinal synaptic action differs from Ia afferent synaptic action by a high potentiation ability during repetitive stimulation. The monosynaptic action is usually followed by less pronounced prolonged polysynaptic effects. It is suggested that the propriospinal pathways under investigation are formed at least partially by axons of cells that are monosynaptically activated in natural conditions by the pyramidal tract and thus represent a link of a disynaptic pathway from the motor cortex to the motoneurones.

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PLASTICITY OF HYPOTHALAMIC GLUCORECEPTORS: A NEW MODEL FOR THE STUDY OF LEARNING AT THE NEURONAL LEVEL. B.I.Kotlyar, T.M.Yeroshenko. Chair of Higher Nervous Activity, Moscow State Univ., Moscow, USSR.

Extracellular recordings were taken from glucosensitive neurons of VMH and LH nuclei of unanaesthetized rabbits during conditioning procedure. All glucoreceptors studied showed plastic changes in their activity when a tone signal (CS) was consistently paired with intracarotid injections (0,25 - 0,30 ml) of isotonic glucose solution (US). The number of trials necessary to produce a noticeable effect depended upon initial reactivity to CS and US and was minimal (10-15), when a response to both stimuli (increase or decrease in discharge rate) has been of the same sign. The stability of conditioned changes was found to be proportional to the number of trials carried out. The results of pseudoconditioning and other controls provide evidence that plastic changes demonstrated were not due to sensitization but were of a true associative nature. The opportunity to bring the US as close as possible to the cell studied, makes glucoreceptors a convenient model for studing mechanisms of plasticity at the neuronal level.

EFFECT OF EPINEPHRINE ON FREE FATTY ACID (FFA) RELEASE BY THE RAT 946 FARALETRIAL RAT BOD! OF NORMAL RATS, IN VIVO. Vanco P. Kovacev and Milica Spasovska. Dept. of Physiology, Med. Faculty, Univ. of Skopje, Yugoslavia.

The parametrial fat body of rat was perfused in vivo, using the method Kovacev-Scow (Am.J. Physiol. 210:1199,1966). The effect of injecting epinephrine on FFA release in vivo was studied in normal rats fasted for 1 day; they were given sc 20-30 ug or 50 ug epinephrine and 5-lo ug. FFA release was significantly increased lo min after sc injection of epinephrine. The rate continued to increase next lo min and remained constant thereafter at about 0.05 uEq/(g fat body X min). FFA release was significantly increased immediately after iv injection of epinephrine. There was also an look increase of blood glucose comparing the initial level. The blood flow through parametrial fat body decreased about 30%. There was also significant decrease in blood ketone bodies.

ANALYSIS OF ACETYLCHOLINE DEPOLARIZATION ON STRIATED MUSCLE. L. Kovács, 947 I. Török. Dept. of Physiology, University Medical School, Debrecen,

It is known since Fatt's experiments /J. Physiol. 111: 408, 1950./ that the end-plate potential evoked by acetylcholine /ACh/ is not only capable of generating spikes but it can spread with decremental character on the extrajunctional area of muscle fiber, causing a reversible depolarization there. The mechanism of this slow depolarization was studied. It has been found that the depolarization becomes more remarkable if the muscles are equilibrated in a chloride-free /sulphate/ Ringer before the ACh treatment. 1 mM ACh produces a depolarization of 19,8-6,5 mV on one of the muscle pairs immersed in normal Ringer, while a depolarization of 58,2-4,8 mV is measured on the other one in sulphate Ringer. This depolarization is Na dependent; the depolarization decreases when the Na conrization is Na dependent: the depolarization decreases when the Na concentration of Ringer solution is reduced from 120 to 0 mM. In Na-free Ringer solution, however, the depolarization does not take place. - 1 mM ACh increases the Na influx of sartorius muscles up to 4-8 times. Tetrodotoxin /10-8 g/ml/ does not modify either the increasing effect of ACh on Na influx or the slow depolarization. The rate constant of K efflux is temporary increased by ACh up to 2,2 times.

EFFECT OF NEONATAL CORTISONE ADMINISTRATION ON MATURATION AND THE POST-948

Physiol., Univ. Med. School, Pécs, Hungary.
The effect of a single s.c. injection of 1 mg cortisone given to male rats on the first post-natal day was investigated on the maturation and the postnatal development of the brain at 7, 14, 21, 35 and 50 days of age. It was found that in each age group the weights of body, brain /cerebrum, cerebellum/ and adrenal glands decreased in the cortisone injected animals in comparison to controls. The weights of anterior pituitary, thyroid gland and testes also decreased except the 7 days old anitary, thyroid gland and testes also decreased except the 7 days old animals. In animals injected with cortisone the mean age at which eye opening occurs was advanced by 2-3 days over that of the controls. Postnatal cellformation in the cerebrum and cerebellum was also affected by cortisone treatment. The DNA content of the cerebrum and cerebellum /ugatom DNA--P/organ/, particularly in the older age groups, was much lower in the cortisone treated animals than those of the controls. EFFECT OF PHYSOSTIGMINE ON SODIUM EFFLUX OF FROG SKELETAL MUSCLE. T. Ko-vács and B. Szabó. Dept. of Physiology, University Medical School, Debrecen, Hungary.

The extensive evidence contained here with respect the effect of physostigmine on 24-Na efflux from Na loaded muscle suggests that its inhibitory action resembles in many respects that of ouabain. In a normal Ringer only 25 % of the efflux is blocked by treatment with physostigmine. The physostigmine-sensitive component is markedly increased in low Na-Ringer. In half Na-Ringer the physostigmine-sensitive part of 24-Na efflux accounts for about 45 % of the total. In Na-free Ringer about 60 % of the efflux is physostigmine-sensitive. The inhibitory effect of physostigmine on Na efflux depends on fibre Na concentration. If Na, is lower than 10 mM the total Na efflux is physostigmine-insensitive. In conclusion the results indicate that physostigmine has no effect on ouabain-insensitive exchange diffusion component of Na efflux, whereas, it can block the ouabain-sensitive net sodium transport.

CELLULAR BASIS OF ENDOTOXIN HYPERSENSITIVITY. T.G. Kováts. Institute of Experimental Surgery, Medical University, Szeged, Hungary.

According to our opinion a natural endotoxin hypersensitivity develops in vertebrates owing to symbiosis and infections with endotoxin producing bacteria. Previously only the toxic nature of endotoxin was stressed. We suggest that endotoxin exerts its deleterious effect in two directions: 1. primary toxicity /susceptibility/ and 2. hypersensitivity. These two mechanisms run parallel in the endotoxin effect. The targets of the primary toxic effect of endotoxin are the adrenergic nervous system and some cellular elements playing a role also in endotoxin hypersensitivity. The cellular targets of endotoxin hypersensitivity may be affected by direct action or by the mediation of immunological mechanisms /naturally sensitized lymphocytes, antibody, complement/. The target cells are: micro-, macrophages, mast cells, platelets and lymphocytes. Endotoxin-caused inhibition of macrophage-migration and the lymphoblast transformation are known as well as the passive transfer of endotoxin hypersensitivity by spleen cells. Our experiment showed that normal rabbit, guinea pig or rat mononuclear peritoneal exudate cells /2-loxlo taken 72 hrs after oil injection/ injected ic. to any of the above animals followed by 50-loo ug endotoxin iv. after 24 hrs result in skin haemorrhage resembling Shwartzman phenomenon. The role of hyperaensitivity and lysosomal enzymos in the above cell-mediated reaction is discussed.

EFFECT OF CHELATING AGENTS ON SARCOPLASMIC RETICULAR FRACTION PREPARED FROM STRIATED MUSCLE. A. Köver and M. Szabolcs. Dept. of Physiology, University Medical School, Debrecen, Hungary.

Sarcoplasmic reticular fractions prepared from striated muscle of fish /Ameiurus nebulosus/ were used in experiments. There was established that the treatment of sarcoplasmic reticular fraction previously adjusted to pH 7,3 under unbuffered medium with EDTA or EGTA solution at final concentrations of 3-12 mM and 0,6-1,2 mM resp. /at 0 and for 10 min./ results in an increase of the cholinesterase activity to the 5-12 times of the original value. It induced also a definite increase of SR-ATPase activity measured without and with additional Ca, in spite of that a reduction of 45-Ca uptake was observed simultaneously. The withdrawal of membrane bound Ca by chelating agents modifies the functional properties of SR-membrane very definitely but it is accompanied only by a minimal solubilization of its components. - Ca ions applied in double concentration of chelating agents prevent the modification of SR-membrane under the treatment described above.

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952 EFFECT OF 3'-5'-AMP AND THEOPHYLLINE ON THE TUBULAR REABSORPTION OF SODIUM AND WATER. G.Kövér and H.Tost. Dept.of Physiology, Semmelweis University Medical School, Budapest, Hungary.

In dogs anaesthetized with sodium pentobarbital, 3'-5'-AMP was infused into the left renal artery at a rate of 1 mg/min, then 1 mg of cyclic-AMP together with 1 mg of theophylline, dissolved in 1 ml of saline, during sustained moderate saline diuresis. (1) in the above dose, cyclic-AMP failed to exert any effect on renal haemodynamics or tubular sodium and water reabsorption; C_{cr} and C_{PAH} were not affected either; (2) when cyclic-AMP was given together with theophylline, RBF increased but C_{cr} did not change, sodium and water excretion were augmented; (3) theophylline produced these changes also when given alone; (4) most likely, cyclic-AMP fails to penetrate the cell membrane; (5) theophylline reduces tubular sodium and water reabsorption; (6) the present findings are inconsistent with the concept that cyclic-AMP and theophylline have similar action on living membranes.

953 DISRUPTION OF SHORT-TERM VISUAL MEMORY BY ELECTRICAL STIMULATION OF INFEROTEMPORAL CORTEX. R. Kovner and J. S. Stamm. State University of New York, Stony Brook, New York, USA.

Four monkeys were trained on visual delayed-matching-to-sample. The monkey sat in a chair facing a panel which contained three windows. For each trial the programmed sequence was: (a) one of two patterns (sample) was displayed in the top window; (b) after S pressed the sample all windows were blank (delay) for 3 or 6 secs; (c) both patterns were displayed in the bottom windows (match-onset) and when S pressed on either window, they were blanked for 8 secs (III). A press to the same pattern as the sample (correct response) was food rewarded. Electrode assemblies were chronically implanted on temporal and prefrontal cortex. In each 150 trial session bipolar electrical stimulation of 2 or 1 sec duration was applied during discrete portions of the trial. Non-stimulation trials were interspersed. Results: (1) correct performance was significantly disrupted only with stimulation of anterior inferotemporal cortex during the delay or at match-onset; (2) the magnitude of the deficit became greater as the stimulation occurred closer to match-onset; (3) no significant deficits were obtained with inferotemporal stimulation during simultaneous-matching (sample remains on); or (4) with prefrontal stimulation. Conclusion: Anterior inferotemporal cortex is critically involved in the mediation of visual short-term mnemonic processes, but not in the utilization of long-term associative or in perceptual processes. (Supported by NSF Grant GB 6911)

INTERACTION BETWEEN HYPOXIA AND VASOACTIVE SUBSTANCE IN THE CORONARY CIRCULATION

T. Koyama, K. Nakagawa and Y. Ikeda. Dept. Physiol. Inst. Appl. Electricity, Hokkaido Univ. Sapporo, Japan.

In view of the experimental fact that the 0_2 consumption of the heart is kept constant even in hypoxia by increasing the coronary blood flow (CorBF), it seemed reasonable that the coronary vasodilating substances would cause more strong effect in hypoxia than in air respiration. In order to examine this expectation, CorBF of anesthetized dogs was measured under hypoxia (6.72%0 $_2$) by use of an H_2 catheter electrode. Strong increases of the heart rate and aortic blood pressure caused by hypoxia were suppressed to some extent by previous application of propranolol or phentolamine. Then carbochromen (Intensain $\mathbb Q$) was intravenously injected in a dose of 2 mg/kg during both air and hypoxia respirations. The coronary vasodilating effect of carbochromen was evalueated by measuring CorBF before and after its administration. As the results it was ascertained that the increase of CorBF caused by carbochromen was 4 times as much in hypoxia as that in normoxia. This observation verified the above expectation. Such a potentiation of vasodilating effect of carbochromen may be explained according to Fick's principle by the assumption that the coronary vasodilating substance acted so as to elevate the cardiac venous P_{0_2} to a definite extent under both hypoxia and normoxia.

SIMILARITIES AND DIFFERENCES IN PLASMA FSH AND LH CONCENTRATIONS IN DEVELOPING MALE AND FEMALE RATS. C.L. Kragt, J.F. Masken and G.J. Bloch. Department of Physiology, University of California San Francisco, San Francisco, California, U.S.A.

Studies indicate that pituitaries of male and female rats store FSH and LH in different amounts and that the differences change with age. Minimal data exists for plasma levels. Blood samples were obtained from the abdominal aorta of Sprague-Dawley male and female rats between 5 and 80 days of age. Plasma FSH and LH concentrations were measured by radioimmunoassay(NIAMD). At 15 days of age, FSH concentrations in the female(1329 ng/ml) are about 4X greater than those in the male (301 ng/ml). LH concentrations are about 3X greater (790 vs 260 ng/ml). In both males and females, the period between 15 and 35-40 days of age was characterized by marked decreases in both FSH and LH. In the male, LH values persisted at low values between 150-325 ng/ml to 80 days of age. Contrarily, FSH values increased 2-3 fold to values between 500-700 ng/ml by 60 days. This increase was followed by a decrease to about 375 ng/ml at 80 days of age. In the adult female, previously reported data indicates that the estrus cycle is characterized by LH titers of about 1500 ng/ml during the evening of proestrus associated with lower levels of FSH(300-500 ng/ml). The data support the suggestion that a "surge" of FSH and LH at about 15 days of age in the female may serve as an "inductive" mechanism leading to reproductive periodicity in adulthood. In the male, divergence of FSH and LH concentrations at the time of puberty suggests the existence of separate neuroendocrine mechanisms controlling their release and further that FSH may initiate puberty. (Supported by Grants AMO 6704, AMO 5613, ASC #06, and MSC #17.

TOTAL BODY WATER, AND WATER SOLUBLE BODY SODIUM AND POTASSIUM IN GOLDBLATT - HYPERTENSION. P.Kramer and B.Ochwadt . Max-Planck-Institute for Experimental Medicine, Department of Physiology, Göttingen, Germany.

32 hypertensive rats with unilaterally constricted renal artery and 20 normo - tensive rats were sacrificed and then dried at 110°C until the weight of the carcasses remained constant. The total weight loss was regarded as total body water. Then the carcasses were homogenized and boiled in aqua bidest, in order to determine the water soluble sodium and potassium. The results are indicated as follows:

	Total body water (% of body weight)	Water soluble body sodium (meq/11 body water)	Water soluble body potassium (meq/11 body water)
Normotensive rats Hypertensive rats	64.6 ± 1.8 p < 0.001 66.7 ± 2.1	71.8 ± 2.7 p < 0.01 69.2 ± 2.8	86.8 ± 4.0 p < 0.05 84.4 ± 4.2

The increased total body water in the Goldblatt rats was already present one week after the clamping operation, before the elevation of the blood pressure. At this time, however, the body sodium per total body water was not yet reduced.

INTRAHEPATIC CIRCULATION AND LIVER FUNCTION. N. Krarup and J. A. Larsen. Inst. of Physiology, University of Aarhus, Denmark.

In experiments on cats anesthetized with chloralose it was observed that a fall in body temperature from 38.5°C-36.5°C induced marked changes in liver function as judged from changes in the elimination rate of glycerol and ethanol, bile secretion and the hepatic uptake of Indocyanine Green. At approximately 37°C the elimination rate of glycerol and ethanol was abruptly reduced by 30-40 per cent, accompanied by a reduction in bile secretion and the hepatic uptake of Indocyanine Green to the same extent. A further reduction of temperature was without significant effect and by raising the temperature the changes appeared to be reversible. Total liver blood flow was unchanged. The observed changes could also be elicited by local cooling of the portal vein and after denervation of the liver. The effect of temperature may be explained by restricted distribution of blood flow within the liver and a corresponding reduction in functional capacity. This explanation is in accordance with previous in vivo observations of liver circulation and is supported by angiographic studies in progress.

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958 ON THE CORRELATION BETWEEN THE ANALYSING AND ACTIVATING SYSTEMS OF THE BRAIN. Yu.G.Kratin. Pavlov Inst.of Physiology, USSR Academy of Sciences, Leningrad, USSR.

According to the usually adopted conception, the activation of the cortex is a function of the stimulus strength, directly depending on the intensity and duration of the impulsation influx pouring into the brain stem, reticular formation through collaterals from the specific afferent pathways. However, the electrical reactions of the non-anesthetized normal brain (in experiments on men, cats, rabbits) suggest that this is true only for the first presentation of a new stimulus. In general, the reflex excitation of different brain systems caused by any signal, and primarily, the excitation of the non-specific regulating mechanisms, is controlled by the action of the analysing apparatus. The latter is interpreted as the functional integration of diverse specific and associative neuronal sets serving the determination of the biological significance of the perceived stimulus. The more complicated the analysis of the given signal - positive or negative - the higher the functional tension of the analysing system, and this is reflected in arousal reactions of the brain through the mediation of the activating mechanism. The dependence is revealed during positive conditioning, differentiation and in other cases.

959 CHANGES IN GLYCOLYTIC METABOLITE LEVELS IN THE FROG MYOCARDIUM IN THE COURSE OF THE HEART CYCLE. E.-G.Krause, A.Wollenberger, E.V.Bogdanova, and E.B.Babskii. Inst. of Circulation Res., German Academy of Sciences, Berlin-Buch, G.D.R., and Inst. of Normal and Path. Physiology, Moscow, USSR.

Hearts of frogs (rana temporaria) were instantly frozen in situ in different phases of the contraction cycle by an automatic cooling device triggered at preset points of the electrocardiogram. Characteristic cyclic changes were seen in the myocardial levels of several glycolytic intermediates: Glucose-6-phosphate, fructose-6-phosphate, fructose-1,6-diphosphate, 3-phosphoglycerate, and pyruvate. The nonequilibrium mass action ratio of the phosphofructokinase reaction exhibited likewise cyclic changes and was highest toward the end of the R wave of the electrocardiogram, indicating peak activation of the enzyme at that time. The activation was coupled with increases in orthophosphate (P; E.B.Babskii et al., Dokl.Akad.Nauk SSSR 171,750,1966) and in the phosphate potential (ADP x Pi/ATP).

PEAK MEASURED ISOVOLUMIC VELOCITY OF SHORTENING OF THE CONTRACTILE ELEMENTS (Vpm) UNDER ACUTE PRESSURE LOAD IN CONSCIOUS MAN. H.P.Krayenbuehl, W.Rutishsuser, M.Schoenbeck and H.Mehmel. Med.Policlinic, Univ. of Zuerich, Switzerland.

It has been suggested that Vpm may serve as an index of myocardial contractility. In order to be a useful measure of contractility Vpm should be independent of preload. It is investigated if in man without signs of grossly abnormal left ventricular (LV) function Vpm as determined from high-fidelity LV pressure curves varies when an increase in preload is induced by elevating acrtic pressure by methoxamine (M). In a first group of 11 cases M led to an increase of LV end-diastolic pressure (EDP) of 7 mm Hg associated with a highly significant decrease of Vpm and heart rate (HR) (P<0.001). LV max.dP/dt remained unchanged. Thus, the decrease of Vpm may have been caused by both an increase in preload and a decrease of contractility. In a comparable second group of 8 patients, given 10 mg propranolol and 1 mg atropine i.v. prior to M in order to minimize cardiac reflex adjustments, a similar increase in EDP was accompanied by a smaller decrease (P<0.05) of Vpm than in group 1. HR remained unchanged whereas max.dP/dt increased significantly (P<0.01). From the observations in group 2 where depression of contractility was unlikely to have occurred it is concluded that Vpm depends on preload. Therefore, Vpm may solely serve as an index of contractility if variations of preload are absent or minor.

ON THE MECHANISM OF THE EFFECT OF ALDOSTERONE ON SODIUM REABSORPTION IN NEPHRON CELLS. T.V. Krestinskaya. Inst. of Evolutionary Physiology and Biochemistry, Academy of Science, Leningrad, USSR.

It is known that aldosterone increases sodium reabsorption in renal

cells, but it is unknown which of the enzymes are involved into this effect and what is the site of aldosterone action in the nephron. In present investigation the effect of aldosterone on the (Na-K) ATPase and some of the dehydrogenases of Krebs cycle was studied cytophotometrically. It was shown that adrenalectomy decreases the activity of (Na-K) ATPase, succinate, malate and isocitrate dehydrogenases both in proximal and distal segments of the nephron. In adrenalectomized animals, aldosterone produces a significant (P<0,02) increase in (Na+K) ATPase and succinate dehydrogenase activities only in the cells of distal convoluted the last of the corporate and succinate dehydrogenase activities only in the cells of distal convoluted tubules. Under the same conditions, no increase has been observed in the activity of malate and isocitrate dehydrogenases in any of the nephron segments. The data obtained indicate that (Na±K) ATPase and succinate dehydrogenase are involved in realization of aldosterone effect on renal sodium reabsorption, and that this effect being located mainly in distal convoluted tubules.

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EFFECT OF NEO- and POSTNATAL ALTERATION OF LIGHT ENVIRONMENT ON CIRCADIAN PERIODICITY OF PLASMA CORTICOSTEROID LEVELS(11-OHCS) IN THE RAT. D.T. Krieger and H.P. Krieger, Mount Sinai School of Medicine, N.Y.C., N.Y., U.S.A.

The circadian periodicity of plasma 11-OHCS levels (over a 48 hour period, sampling q.4 hrs.) was determined in groups of animals raised under varying light-dark (LD) conditions from birth until time of sacrifice at 30 or 80 days of age. (1) Animals raised in constant light(CL), constant dark(CD) or enucleated at 1 day of age, do not show normal periodicity when sacrificed at 30 or 80 days of age. (2) Animals raised in CL until 20d. of age, then shifted to normal LD, do not demonstrate normal periodicity at 30 days but have normal periodicity at 80 days. (3) Animals raised in normal LD until 14 days and either then enucleated or raised in CL or CD do not show normal periodicity at 30d. (4)Animals raised in normal LD until 30d. and either then enucleated or raised in CL do not show normal periodicity at 80d. These results indicate (a)that exposure to an abnormal light-dark environment can disrupt circadian periodicity despite prior exposure (for either 14 or 30d.) to normal LD; thus, there is no evidence for "imprinting of such periodicity; (b)that neonatal exposure to CL does not permanently disrupt circadian periodicity, since such periodicity returns after a suitable subsequent exposure to normal light-dark alternation.

LYSOZYME ACTIVITY IN THE DENERVATED FROG MUSCLES. R.V.Krishnamoorthy, Dept. 963

Lysozyme (EC 3.2.1.17) in the sartorius and gastrocnemius muscles of frog Rana hexadactyla was isolated by ion exchange (Dowex 50 W x 2) chromatographic fractionation. Adecrease in the order of o.oo1 O.D.per min.per mg protein at 450 mu when the enzyme is added to the suspension of Micrococcus lysodeikticus was considered as the specific activity unit. These muscles in both legs of a normal frog showed the same activity. The enzyme in the eluant was stable at 100°C for 3 min.and at pH 4.6. Rise in pH destroyed the activity of the enzyme. When the sciatic nerve root of one leg was surgically denervated for 1 month , the activity increased in these atrophic-denervated muscles by 1.5 to 2 times greater than those of innervated contralateral controls. Sham-denervated frogs for 5 min.did not vary the enzymic activity due to sciatic denervation. The increase in the lysozyme activity in these atrophying muscles was steady upto 3 months of denervation; the latter results in 28±2.5% atrophy in gastrocnemius and 15±3.2% atrophy in sartorius. The increase was more pronounced in gastrocnemius than in sartorius. As a pathophysiological parameter, the increase in lysozyme activity puts up a premium with the

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wasting processes of denervation-atrophy.

964 POWER FUNCTIONS AND INFORMATION TRANSMISSION IN TYPE I AND II SLOWLY-ADAPTING MECHANO-RECEPTOR NEURONS. L. Kruger and B. Kenton. Dept. of Anatomy and Brain Research Inst.,

Univ. of Calif., Los Angeles, Calif., USA.

The quantitative relations between impulse discharge and skin displacement were studied in first and second order neurons representing cutaneous slowly-adapting mechanoreceptors in cat hindlimb. The transformation of S-shaped functions into linear or power functions describing the dynamic range is influenced by several factors capable of inducing large fluctuations in power function exponents which preclude meaningful direct comparison between neurophysiological and psychophysical data. Experimental observations suggest that central neuronal processing is not a net linear model. It is also demonstrable that information transmission levels below channel capacity for individual neurons exceed the number of discrete discriminable levels deduced from human subjective magnitude estimation. Supported by USPHS Grant NB-5685.

965 THE DISTRIBUTION OF HYPOTHALAMIC HYPOPHYSIOTROPIC FACTORS IN THE HYPOTHALA-MUS OF THE RAT. L. Krulich, M. Quijada, P. Illner, S.M. McCann. Univ. of Tex. Sw. Med. Sch., Dept. of Physiology, Dallas, Texas 75235, USA.

Freshly frozen hypothalami from normal male rats were serially sectioned at 400 µ along the frontal, sagittal and horizontal planes and the individual portions extracted with 0.1 N HCl. The content of releasing and inhibiting factors of these extracts was estimated in an in vitro system (6 pituitary halves incubated for 3h in medium 199) from the release of TSH, LH, FSH, prolactin and GH measured by specific radioimmunoassay. Significant accumulations of TRF were found in the dorsal mediolateral part of the preoptic area and in an area extending from the median eminence into the dorsal mediolateral part of medial hypothalamus. The bulk of the LRF and FRF activities was confined to a thin ventromedial portion of medial hypothalamus (median eminence and pituitary stalk). Lesser activity was also found in the ventromedial part of the preoptic area. Significant PIF activity occurred in the dorsalateral portion of the preoptic area. Extracts from the median eminence increased prolactin release. Preliminary results indicate presence of both GRF and GIF. Their exact localization is now under investigation.

VMI-20-4, A NORADRENALINE RELEASING COMPOUND. I.M.Krushkov, D.S.Paskov. Dept. of Pharmacology, Higher "edical Institute, Sofia, Bulgaria 966

A pyridin derivate of a continuous hypertensive effect has been investigated. Experiments have been carried out on different kinds of animals, investigating the effect of the compound on the arterial pressure, on the cardiac rythmicity under different kinds of narcosis, on sure, on the cardiac rythmicity under different kinds of hardesis, on the blood flow in different vascular regions, on the smooth-muscular organs. The analysis of the mechanism of action shows that the compound VMI-20-4 causes release of noradrenaline, but has also a direct exciting effect on the alpha-adrenergic receptors in the effector organs.

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DELAYED ALTERNATION PERFORMANCE AND THALAMIC UNITS IN RHESUS MONKEYS.
K. KUBOTA, H. NIKI AND A. GOTO. Dept. of Neurophysiology, Primate Research Inst., Kyoto Univ., Inuyama, Aichi, Japan, 484.

In a previous report (J. Neurophysiol., In press, 1971) unit activity was recorded from the dorsolateral prefrontal cortex during spatial delayed alternation lever-pressing performance in the rhesus monkey. kinds of unit activities were found: one was active during delay phase and the other was active several hundred msec preceding to lever pressing. was attempted to analyze how neurons in the thalamus are involved in the performance of the delayed task. In four rhesus monkeys discharges of thalamic units were recorded and compared with those in the prefrontal Units in the dorsomedial nucleus increased their rate immediately cortex. before lever pressing. Their temporal sequence was similar to the units in the cortex. Different from the prefrontal cortex, no units were found which are active only during the delay phase. Units in the ventrolateral nucleus were active almost synchronous with an onset of the triceps brachii EMG whenever an animal pressed levers. These results are consistent with a notion that the dorsomedial nucleus of the thalamus is involved in the initiation of the delayed performance and convey an excitatory influence to the dorsolateral frontal cortex.

INVESTIGATIONS OF THE ELECTRIC FIELD OF ACTIVATED SKELETAL MUSCLES IN MAN BY MEANS OF SURFACE ELECTRODES. G. Küchler and H. Kramer. Inst. of Occupational Medicine, Dept. of Work Physiology, Berlin, GDR.

Investigations were made in order to determine the integrated electrical activity, derived in unipolar or bipolar way from various positions of activated muscles (biceps and triceps brachii). (1) In experiments with a unipolar derivation a maximum of recorded mean electrical activity was found above the belly of the muscles. (2) The level of the bipolar recorded electrical muscle activity was highest at an electrode distance of about 8 cm. The results are discussed in respect to the conduction velocity of the action potentials in muscle and the mean frequencies occurring in the electromyogram.

PHYSIOLOGICAL SIGNIFICANCE AND MECHANISM OF ACTION OF HEPARIN COMPLEX COMBINATIONS WITH FIBRINOGEN, EPINEPHRINE AND NOREPINEPHRINE BY THE REGULATORY REACTIONS OF ANTICOAGULATING SYSTEM. B.A.Kudrjashov. Dept.of Physiology Moscow University, Moscow, USSR.

The tolerance of animal organism to thrombin has been shown to depend upon the function of anticoagulating system (Thromb.Diathes.haemorrh.6,371, 1961). The appearance of thrombin in blood stream leads to a rise in anticoagulant and fibrinolytic potentials in consequence of the reflex excretion of heparin and activator of plasminogen into blood stream from the tissue depot. Heparin forms complex combinations with fibrinogen, epinephrine and norepinephrine in vivo and in vitro. All these complexes inhibit the polymerization of fibrin monomer and stabilization of fibrin. They carry out the lysis of non-stabilized fibrin. Antiplasmin and EACA do not block this activity. These complexes have been discovered in the blood of animals after an intravenous injection of thrombin. They have been found in the blood of young people after emotional tension or by some diseases accompanied by pain. The complexes accomplish apparently the natural prophylaxis of thrombosis. The facts obtained by the study of activity of the complexes, requires distinction on 2 forms of natural fibrinolytic activity in the organism: enzymatic and nonenzymatic.

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970 VASOPRESSIN PLASMA LEVELS IN THE LACTATING GOAT AFTER VAGINAL DISTENSION.

E.R.Kuhn & G.Peeters. Dept. of Physiology, Veterinary Faculty, Univ. of Ghent, Belgium.

The release of oxytocin and vasopressin after vaginal distension has been evaluated previously by simultaneous occurence of milk ejection and antidiuresis in the hydrated lactating goat. Meanwhile, increased plasma levels of oxytocin have also been demonstrated during this stimulus. In the present experiments blood samples were taken from an indwelling catheter in the jugular vene and vasopressin was estimated in plasma of the lactating non hydrated goat using TCA-extraction and purification with XE-64 resin column chromatography, followed by the ADH assay in water loaded, ethanol anesthetized rats. Mild vaginal distension increased the plasma levels of ADH dramatically in 11 out of 13 assays in 5 different experiments using two different animals which have been pretreated with Largactyl in order to avoid stress. During the vaginal distension stimulus, which lasted for one minute, milk ejection was observed.

971 CHANGES IN CATECHOLAMINE EXCRETION AS THE CONSEQUENCE OF SLEEP DEPRIVATION. V.Kujalová, E.Kuhn, V.Brodan. Inst. of Hygiene and Epidemiology and Inst. of Clinical and Experimental Medicine, Prague, ČSSR.

In a group of 6 men hospitalized during the experiment changes in excretion of noradrenalin and adrenalin were followed up during a period of 5 days of sleep deprivation. The total period of lasting of the experiment including the control period before and after the experiment was 12 days. The level of vigilance was continuously controled by a working group composed of clinicists, a psychiatrist and psychologist. Since the first day of the experiment the experimental persons were given balance diet into 8 meals between the 7th.-24th. hour with sufficient supply of liquids. Urine was collected at 3 hour intervals. The experiment took place without complications. The greatest deviation from the mean value of excretion of noradrenalin was recorded on the 4th day and of adrenalin on the 3rd. day of sleep deprivation. There appear between the individual persons considerable interindividual differences in the excretion of catecholamines already during the rhythms in the control period and these differences become more significant in the course of sleep deprivation. The mean increase of noradrenalin during the entire period of sleep deprivation reaches 31%, with adrenalin 56%; it is significant in both cases. If however evaluating the deviation during the individual days of sleep deprivation the differences are many times over. The changes in the excretion of catecholamines in the individual persons are directly related to the results of psychological tests, affecting the basic character of their personality.

972 EXCITATION OF POSTEROMARGINAL CELLS (LAMINA I) IN MONKEY AND THEIR PROJECTION IN LATERAL SPINAL TRACTS. Kumazawa, T., Perl, E. R., Burgess, P. R. and Whitehorn, D. Dept. Physiol., Univ. Utah Col. Med., Salt Lake City, Utah, 84112, U.S.A.

In cat, cells of lamina I of the spinal dorsal horn have been shown to receive a specific input from nociceptors and thermoreceptors of the skin (Christensen, B. N. and Perl, E. R., J. Neurophysiol. 33: 293, 1970). The techniques of that study were used in the present work on the monkey: a search for discharges from dorsal horn neurons evoked by afferent volleys only when they contained impulses conducted under 35 m/sec; testing such units by quantitative mechanical and thermal stimulation of the skin; marking the location by electrophoretically deposited dye from the recording microelectrode. determine projections of units so identified, electrodes on or in the spinal white matter permitted tests for antidromic activation from rostral regions. Specific nociceptor and thermoreceptor connections to lamina I neurons in monkeys were readily demonstrated; the marginal cell system is better developed in the primate than in the carnivore, notably in the number of thermoreceptive neurons. About 25% of coccygeal marginal units in the monkey (and in cat) could be antidromically excited from the crossed lateral column at the upper cervical level. The axonal conduction velocities in the lateral column ranged from 2 to 30 m/sec. It is concluded that fibers from lamina I cells contribute to the lateral column tract important for pain and thermal sensation. Supported by USPHS grant NS 01576.

SYNAPTIC RESPONSES OF SPINAL MOTONEURONS EVOKED BY INTERNUNCIAL IMPULSES. M. KUNO and J. N. WEAKLY. Dept. of Physiol. Univ. of Utah Med. Ctr., Salt Lake City, Utah, U.S.A.

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Synaptic potentials were recorded intracellularly from lumbosacral motoneurons of the cat following stimulation of interneurons by a pair of fine electrodes inserted into the spinal cord. To confine the stimuli to interneurons, the descending tracts and primary afferent fibers were previously degenerated by chronic spinal hemisection and dorsal rhizotomy. Intraspinal stimulation produced monosynaptic EPSPs and IPSPs in motoneurons, depending on the location of the stimulating electrodes. At a fixed stimulus intensity, both EPSPs and IPSPs showed a random fluctuation in amplitude with occasional failures. The number of lailures and the amplitude fluctuation often remained unchanged at different stimulus levels. In such cases, the amplitude fluctuations cannot be attributed to changes in the number of interneurons stimulated. In addition, when two identical stimuli were applied successively at short intervals (2 - 20 msec), the average amplitude of the second synaptic response was significantly (up to two times) greater than that of the first. This facilitation was associated with a decrease in the amplitude fluctuation as well as in the number of failures. It is concluded that the release of transmitter by both excitatory and inhibitory internuncial impulses occurs in quantal steps (supported by USPHS grant NS 07391).

CHANGES OF ADRENERGIC REACTION PATTERN IN EXPERIMENTAL DIABETES; G. Kunos H. Szentiványi, Regina Cseuz. IIId Dept. of Medicine, Semmelweis Medical University, Budapest, Hungary.

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Aortic strips taken from alloxan-treated diabetic rabbits showed increased noradrenaline /NA/ sensitivity when compared to controls. Whereas in the controls NA contractions could be blocked only by alpha blocking agents, in diabetes both phentolamine /5X10-7/ and propranolol /5X10-7/ produced a significant and parallel shift to the right of the NA dose-response curve. This effect of propranolol proved to be specifically bound to its beta blocking capacity. Isoproterenol, causing contractions in the controls in high doses only, became effective in diabetic preparations already in its "beta-stimulant" dose range. On cold storage of the preparations for 24-48 hours NA sensitivity remained increased, whereas the capacity of propranolol to inhibit NA contractions disappeared in the diabetic preparations. Pretreating normal rabbits with prednisolone to simulate increased adrenocortical activity in diabetes also enhanced NA sensitivity but no beta sensitivity of catecholamine constriction had appeared. The appearance of a beta constrictor response in diabetes in an organ with predominating alpha receptor activity is discussed in relation with previous findings showing qualitative changes in the adrenergic receptor mechanism on alterations of the metabolic milieu.

EFFECT OF CONTROLLED DELAYS IN AN EXTERNAL RESPIRATORY FEEDBACK LOOP. A. L. Kunz, R. M. Weissburg and D. A. Miller. Department of Physiology, The Ohio State University, Columbus, Ohio 43210, U. S. A.

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Using awake, unidirectionally respired chickens, ventilatory flow was maintained constant at 5 L/min. (9 x normal). $\rm CO_2$ concentration of the inspiratory gas was controlled by an electropneumatic transducer modulated by a computer. Respiratory movements monitored by a whole body plethysmograph feedback to the computer to control $\rm CO_2$ concentration using the algorithm % $\rm CO_2(t)=\int [\dot{Q}-\dot{V}_{1(t-\eta)}]dt$. This system produces an alveolar $\rm CO_2$ concentration which increases continuously proportional to the analog of $\rm CO_2$ production (\dot{Q}) and is brought down in increments proportional to the inspiratory ventilation (\dot{V}_1) after a delay of τ sec. The net effect of this feedback was to produce a dynamic equilibrium of alveolar $\rm CO_2$ concentration oscillating ±1% about a mean value of ½-5% at the frequency of respiration. The question asked by this set of experiments was what effect does delay in the information loop have upon ventilation? We found that short delays (less than 2 sec.) produced a slower respiratory rate and a deeper tidal volume. Long delays (greater than 6 sec.) cause undulating instability similar to Cheynne-Stokes respirations. This would indicate an importance of the temporal relationship between alveolar $\rm CO_2$ oscillations and the phase of respiration. (Supported in part by 0.N.R. Grant N.R. 101-733.)

976 STUDIES ON THE ACTIVITY OF GROWTH HORMONE RELEASING HORMONE OF THE HYPOTHALAMIC EXTRACT BY THE "PITUITARY DEPLETION METHOD". M. Kurcz and I. Nagy. Dept. of Biochemistry and Isotope, National Institute of Public Health and Heim Pal Children's Hospital, Budapest, Hungary.

Bioassay /tibia test/ has revealed that the growth hormone /GH/ content of the rat pituitary decreases in response to stress effects, insulin, vasopressin and hypothalamic extracts. These observations suggested the elaboration of "Pituitary Depletion Method" for assaying GH releasing hormone. Radioimmunoassay has not confirmed the decrease in anterior pituitary GH content. - Therefore, we studied the changes in anterior pituitary GH by a novel, objective biochemical method: acrylamide-gel electrophoresis. The experiments showed that acute stress effects and the administration of different drugs, further hypothalamic extracts prepared by various methods did not induce any change in pituitary GH levels. These data indicate that the "Pituitary Depletion Method" is unsuited for the quantitative determination of the GH releasing hormone. The pituitary contains GH in amounts manifold that of the blood. Thus, the pituitary can be regarded upon as an organ of storage which releases only some per cents of its GH content in response to acute physiologic or non-physiologic stimuli. The decrease in hormone content cannot be recorded by any of the known methods. Some doubts arise concerning the adequacy of the 20 to 60 per cent decrease measured in bioassay.

977 PROTEIN AND AMINO ACID METABOLISM IN THE DICESTIVE TRACT OF RUMINANTS. N. V. Kurilov

A.N. Kosharov, A.M. Materikin, A.A. Ptashkin, A.M. Solovyov, L.V. Kharitonov.

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It was studied the nitrogenous metabolism in the lumen and the wall of digestive tract by the use of stable and radio active indicator and immunological precipitation method. It was shown the entering of endogenous protein (enzymatic and blood plasma protein) in all compartments of digestive tract, the dependence of this process upon the age and physiological stage, the possibility of temporary deposit of nitrogen in the wall especially during pregnancy and lactation. As fast as endogenous protein moves in the distal direction it is broken and the amino acids formed are absorbed into the blood. Food and blood proteins protect the digestive tract enzymes from the rapid destruction. The digesting proteins of food, endogenous proteins and amino acids entering from blood form in the lumen an optimal mixture for the absorption. In the process of absorption it takes place the transamination of a part of amino acids, the utilization of newly-formed amino acids for the synthesis of enzymes or cellular protein. Rumen and intestinal wall can also utilize urea or ammonium salt nitrogen for the amino acid synthesis. The level of transmination processes and the amino acid synthesis in the wall depends on the correlation of absorbed amino acid mixture to the requirements of the following synthesis.

STUDIES ON THE PATHOGENESIS OF METABOLIC ALKALOSIS (MA). N. A. Kurtzman, M. G. White, and P. W. Rogers. USA Inst. of Surgical Research, San Antonio, Texas, USA.

MA was induced in dogs receiving 35 mEq NaHCO3 and 17 mEq NaCl daily by administering K+ exchange resin and DOCA 20 mg daily. MA alkalosis could be fully corrected by either discontinuing DOCA administration or by substituting 35 mEq of KHCO3 for the NaHCO3. MA alkalosis could not be induced by this technique, when less than 10 mg of DOCA was given daily. MA did not develop when 85 mEq NaCl was given instead of 17 mEq. Thus, K+ deficiency without extracellular volume (ECV) depletion, when accompanied by increased amounts of mineralocorticoid, is a sufficient stimulus for the development of MA.This tendency of K+ deficiency to induce MA can be completely overcome if ECV is sufficiently expanded with NaCl. In this model, proximal tubular HCO3 reabsorption is not stimulated as the effect of DOCA induced salt retention and ECV expansion counterbalances the effect of K+ depletion on proximal HCO3 reabsorption. MA developed in adrenalectomized animals, ECV depleted with furosemide and treated with an electrolyte free diet and dexamethasone, receiving 20 mg/day of DOCA; when 0.5 mg/day was given MA did not develop. MA could be maintained in these animals if the dose of DOCA was reduced to 0.5 mg following the generation of MA. MA results from K+ depletion or ECV depletion (alone or in combination). Hyperaldosteronism is necessary for the kidney to generate MA. Hyperaldosteronism is not required for the kidney to maintain MA if a stimulus to increased proximal reabsorption is present.

THE CORRELATION BETWEEN EXTRAVASCULAR pH AND PIA ARTERIAL AND ARTERIOLAR RESISTANCE IN CATS. W. Kuschinsky and M. Wahl. Dept. of Physiology, University of Munich, Germany.

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Recently it has been demonstrated. that HCO3 free isotonic mock spinal fluid dilates pia arteries locally when microinjected into the periarteriolar space. Solutions containing 25 meq/1 HCO3 and more induced a segmental constriction. In the present study the effect of different HCO3 concentrations was quantitatively analysed. The changes in vascular diameter were measured from photographs taken during the perivascular application. At HCO3 concentrations between 0 and 22 meq/1, a reverse relationship between HCO3 concentration and vessel diameter was found: 0 meq/1 HCO3 increased the vascular diameter by 41.6%, 5 meq/1 HCO3 by 25.0%. At HCO3 concentrations of 11 and 14.5 meq/1 variable results were obtained, the mean values being not statistically different from controls. Solutions containing 22 meq/1 HCO3 always constricted (mean decrease of diameter 17.9%). When catecholamines are applied in mock spinal fluid which itself has no vascular effect, vasoconstriction occurs. This constrictory effect is overridden by the dilatory effect of low HCO3 concentrations. These data indicate that cerebral arteriolar resistance is preferentially controlled by extravascular pH.

"Wahl,M.,P.Deetjen,K.Thurau,D.Ingvar,N.A.Lassen,Pflügers Arch.316,15X1970)

CHANGES IN MYOCARDIAL REPOLARIZATION ASSOCIATED WITH CHANGES IN CONTRACTION.

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A feedback between contraction of cardiac muscle and its electrical activity has been demonstrated in intact isolated frog heart, papillary muscle, and mammalian heart in situ. Isometric or isovolumic myocardial contraction shows faster repolarization than isotonic contraction. But in the intact isovolumic ventricle this faster repolarization phase, as recorded by a suction electrode, is interrupted by a hump-like after-potential which may reach threshold and initiate a propagated action potential. Similar electrical events can be obtained when a microelectrode recording is made from an isometrically contracting papillary muscle if it undergoes a "quick release" during the decline of its active state. Out-of-phase movements of the epicardium found during isovolumic contraction may produce mechanical conditions analogous to the quick release. The same mechanism may give rise to changes seen in action potentials of intact or isolated cardiac muscle.

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CYCLIC AMP AND CONTROL OF PITUITARY PROTEIN SYNTHESIS AND RELEASE. F. Labrie, A. Lemay, S. Lemaire, G. Poirier, R. Boucher, N. Barden, A. De Léan and M. Gauthier. Lab. of Molecular Endocrinology, Dept. of Physiology, Fac. of Med., Laval Univ., Quebec, Canada.

Bovine pituitary adenyl cyclase has been purified 25-40 fold and its activity is stimulated by synthetic TRH (Abbott) in partially purified membrane fractions. Proteins with high affinity binding sites for cyclic AMP and cyclic GMP are found mainly in the 200,000 g supernatant and the microsomal fractions. Cyclic AMP-dependent protein kinase was purified from bovine pituitary glands. Cyclic AMP has no effect on the Km for ATP or histones but increases the Vmax of protein kinase activity by 3-6 fold. Dibutyryl cyclic AMP (5 mM) causes a 50 to 80% increase in the rate of incorporation of radioactive amino acid(s) into proteins after 2 to 3 hrs of incubation of rat adenohypophyseal tissue. Concurrently, up to 30 min. after addition of the cyclic nucleotide, there is a 200-300% stimulation of newly synthesized protein released into the medium, the effect being already maximal at 4 minutes. The stimulating effects of dibutyryl cyclic AMP on protein synthesis and release are independent as shown by an undiminished stimulatory effect of the cyclic nucleotide on protein synthesis when the effect on release of secretory proteins is blocked by removal of Ca⁺⁺ from the medium by EGTA or combined increase of Mg⁺⁺ and absence of Ca⁺⁺. Actinomycin D, at a dose which inhibits RNA synthesis to less than 5% of the control rate, is without effect on the stimulatory action of dibutyryl cyclic AMP on either total protein synthesis or release. These data provide strong support for a role of cyclic AMP as mediator of the action of the hypothalamic adenohypophysiotropic hormones. (Supp. by the MRC)

THE "IN VITRO"BIOSYNTHESIS OF ESTROGENS FROM LABELED PRECURSORS BY BOVINE GRANULOSA AND THECA CELLS.E.Lacroix, W.Eechaute, G.Demeester and I.Leusen. Lab. of Normal and Pathological Physiology, Univ. of Ghent, Belgium.

Granulosa and theca cells from ripening follicles of cow ovaries were incubated for 2 and 4 hrs, at 37°C in Krebs-Ringer containing one of the following labeled $^{14}\mathrm{C}$ or $^{2}\mathrm{H}$ steroids: pregnenolone, progesterone, $17\alpha-$ OH-pregnenolone, $17\alpha-$ OH-progesterone, dehydroepiandrosterone, androstenedione. Labeled estradiol, estrone and other steroid intermediates produced were extracted with methanol, purified and separated by column and paperchromatography and estimated by radiochromatogram scanning and liquid scintillation counting. All precursors were transformed to some extent to estradiol and estrone by the separated cells as well as by the recombined cells; the transformation was highest with androstenedione and very low with progesterone as precursor. With pregnenolone, $17\alpha-$ OH-pregnenolone and dehydroepiandrosterone as precursor, more estrogens are produced by the recombined cells than by the separated cells together. The results indicate that the biosynthesis of estrogens from pregnenolone proceeds rather via the $\Delta5-$ pathway than via the $\Delta4-$ pathway.

983 PHYSIOLOGY OF LEARNING AND INFORMATION STORAGE IN FISH. S.K.Lal. Physiology Department, J.I.P.M.E.R., Pondicherry-6, India.

Formation and synthesis of proteins may be concerned in learning and memory storage in the neurons and comparisons have been drawn between immunological memory and in learning and memory storage. Goldfish were trained for colour discriminations. The optic lobes were exposed under narcosis and small bits were removed and homogenised with Freund's adjuvant. After the fish recovered, in the experimental group the homogenate was injected. In the controls, it was confirmed that operation and narcosis have no influence on memory. In the injected animals, memory was not preserved and retraining did not restore the performance to pre-operation pre-injection criterion levels.

TREMOR INDUCED BY HARMALINE IN THE DECEREBRATE CAT. Y. Lamarre and L.A. Mercier Centre de Recherche en Sciences Neurologiques, Université de Montréal, Montréal, Canada.

Harmaline can induce or aggravate the rest tremor in the monkey with mesencephalic lesions. We studied the effect of this drug in 25 unanesthetized and decerebrated cats. Harmaline induces tremor at the frequency of 9 to 12 cps mainly in the flexor muscles. This tremor has a central supra-spinal origin because: (1) transection of the spinal cord at mid-thoracic level abolishes tremor in the hind limbs; (2) tremor is not supressed by dorsal roots section; (3) the motoneurones are still firing rhythmically in the paralysed animal; (4) the anterior lobe of the cerebellum and the bulbar reticular formation show rhythmic activity in relation with the peripheral tremor; (5) the cerebellar and bulbar rhythmic activity is still present in the paralysed and "encephale isolé" animal; (6) destruction of the anterior lobe of the cerebellum or of the fastigial nuclei abolishes the tremor. (Research supported by the Medical Research Council of Canada).

VENTILATORY RESPONSE TO CO_2 DURING PROLONGED CONTINUED STATIC CONTRACTIONS. O.Lammert and B.Rasmussen. Laboratory for the Theory of Gymnastics, University of Copenhagen.

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The purpose of this investigation was to compare the ventilatory response to CO₂ breathing during rest (sitting position) with the CO₂ response during prolonged continued static contractions. Six subjects performed continued static contractions with their legs (5-10% of max. isometric strength) for 20 min, seated on the floor, knees flexed 90°. The ventilation (VE,BTPS) was determined by the Douglas bag method. PaCO₂ and pH were determined from arterialized capillary blood using Radiometer's electrode systems. Blood samples were taken from a preheated fingertip. The sampling of expiratory air and blood started after 30 min of rest, breathing a mixture of CO₂ and normal air. Without interrupting the CO₂ breathing the static contractions were performed. Between the 10th and the 20th min. of static contractions samples were collected for the determinations of VE,BTPS, PaCO₂ and pH. The results obtained on all the subjects showed that with the same increase in PaCO₂ the AVE,BTPS was the same during rest and static contractions. It is concluded that the unchanged ventilatory response to CO₂ from rest to prolonged continued static contractions is in accordance with the response from rest to dynamic work. (Asmussen and Nielsen 1957).

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MEASUREMENT OF THE DETECTION THRESHOLDS FOR VIBRATORY STIMULI IN HUMANS AND MONKEYS; A COMPARISON WITH THRESHOLD EVENTS IN MECHANORECEPTIVE FIRST ORDER AFFERENT NERVE FIBERS. R. H. LaMotte, G. Carli, and V. B. Mountcastle, The Johns Hopkins University, Baltimore, Maryland, USA.

We compared directly in an identical experimental pattern the capacities of monkeys and humans to detect oscillatory mechanical stimuli delivered to their hands via 3 mm probe tips. Monkeys were trained in a variable delay, reaction time paradigm to indicate stimulus detection. They were then exposed, for each frequency, to a matrix of stimulus amplitudes centered around anticipated threshold. Psychometric functions were constructed and their 50% points taken as thresholds. Over the range 2-400 Hz monkeys and humans possess similar thresholds for vibratory stimuli. Intra- and intermanual transfers are accomplished quickly by each with only minor shifts in threshold. Reaction times are identical in the two species: 450-500 msec at threshold, and drop asymtotically to 300-350 msec for strong stimuli. These results are compared with those of a new study of the two sets of myelinated fibers innervating the glabrous skin of the monkey hand thought essential for vibratory sensibility (cf Talbot, et al., J. Neurophysiol. 1968), with parameters set to match the present psychophysical experiments. The detection thresholds overlap those at which peripheral fibers are entrained to periodic discharge by sine wave mechanical stimuli. The activity evoked by weaker stimuli may account for the atonal interval described by human observers. (Supported in part by USPHS Grant 5 POI NSO 6828).

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PRESYNAPTIC POLARIZATION AND THE MOVEMENT OF SYNAPTIC VESICLES.

E.M. Landau and S. Kwanbunbumpen. Dept. of Physiology and Pharmacology,
Tel-Aviv University Medical School, Tel-Aviv, Israel and Dept. of
Physiology, Mahidol University, Thailand.

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When mammalian nerve terminals were depolarized electrotonically, a marked accumulation of synaptic vesicles occurred in the endings. Electrotonic hyper-polarization had the opposite effect.

These results, taken in conjunction with the effects of electrotonus on spontaneous transmitter release, indicate that presynaptic inhibition and inhibition by cathelectrotonus cannot be explained by the repulsion of vesicles from the presynaptic membrane. 988 REINNERVATION OF THE FROG SARTORIUS MUSCLE BY PARASYMPATETIC VAGAL FIBERS. Lynn Landmesser. Dept. of Zoology, UCLA, Los Angeles, Calf.; & Dept. of Physiology, University of Utah, Salt Lake City, Utah 84112, U.S.A.

Properties of frog sartorius muscles, transplanted to the thoracic region and reinnervated by the gastric vagus nerve, were studied for periods of up to 475 days. Vagalinnervated muscle fibers did not atrophy; mean muscle fiber diameter and maximal tetanic
tension per unit cross-sectional area remained normal. No alterations occurred in intrinsic contractile properties or in passive electrical properties, nor were any alterations.
in muscle fiber ultrastructure observable. Excitatory junctional potentials were multicomponent; were of long latency and low quantal content, and showed long-lasting facilitation. The various EJP components could often be separated by stimulus gradation, indicating polyneuronal innervation. They were often of similar time course and EM observations showed bundles of unmyelinated, small-diameter fibers with vesicle-filled varicostites, making contact with muscle fibers almost exclusively at old endplate areas. These
were recognized by the persistence of junctional folds. Acetylcholinesterase gradually
disappeared from the old junctional areas and was not restored by vagal innervation. Vagal-evoked EJPs were consequently not prolonged by anti-cholinesterases. It is concluded
that at least several trophic factors must exist. The vagus nerve contains those factors
necessary to prevent atrophy and maintain muscle ultrastructure. However, it lacks those
factors required to cause alterations of contractile properties or of electrical characteristics of the membrane, and those needed to induce postjunctional acetylcholinesterase.

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SCANNING ELECTRON MICROSCOPY OF THE VESTIBULAR SENSORY APPARATUS OF THE WHITE KING PIGEON.

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2000, Downsview, Ont. Canada.

Our present knowledge of the microscopic anatomy of the pigeon's vestibular apparatus comes primarily from the pioneering light microscopic studies of Hasse (1867), Retzius (1884) and their successors. In recent years, the advent of the scanning electron microscope (SEM) has given the scientist a powerful new tool and which the surface topography of specimens may be studied in greater detail. A SEM was used in the present study to examine the surface morphology of the vestibule of the White King pigeon. High resolution photomicrographs were obtained which show the shapes, cytoarchitecture, and interrelations of the following structures: the cristae ampullaris, the plana semilunata, the septa cruciata and the transverse septa of the semicircular canals; the maculae of the otolith organs; and the macula neglecta. Observations from the SEM photomicrographs, coupled with those obtained from standard light microscopic techniques, enable certain conjectures to be made regarding the relation between structure and function of the components in the pigeon vestibule. These conjectures are presented.

VASCULAR CONDUCTANCE OF MUSCLE, PRIMARY DETERMINANT OF MAXIMAL OXYGEN UPTAKE IN EXERCISE.

M. Landowne and J. Vogel, U. S. Army Res. Inst. Env. Med., Natick, Mass., U.S.A.

Oxygen uptake (0), cardiac output, blood pressure, arterial (A) and femoral venous (V_F) oxygen content were measured in 6 subjects at rest and 3 levels of exercise at sea level (SL) and simulated 4 Km altitude. Blood flow to exercising muscles (Q_E) was estimated as $OE/(A-V_F)$, where OE = O-Obasal; and used to derive conductance (1/resistance) and relative equivalent radius ($r_E=1$ at SL, resting) of the vascular segments participating in exercise. For each subject, the relation of Q_E to O was curvilinear, Q_E exhibiting a significantly decreasing slope with increasing O. This tendency for flow to become limiting is described by the averaged data; $Q_E(L/min) = 25.4-25.6 e^{-.351} OE(L/min)$, residual deviation (RD) = 124. It is emphasized by $\hat{T}_E = 2.52-1.52 e^{-1.63} OE$ (RD= 104) at SL; and the influence of hypoxia constrained to the same limit by $\hat{T}_E = 2.56-1.42 e^{-1.73} OE$ (RD= 234) at altitude. These data suggest that anatomical as well as functional size and number of blood vessels supplying muscle impose a limit to blood flow, which in turn, primarily determines the cardiac output and oxygen transport of healthy individuals. Under these circumstances, maximal oxygen uptake does not reflect ventilatory, myocardial or diffusional limits.

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INTRACARDIAC AND INTRAVASCULAR RECORDING OF DYE DILUTION CURVES WITH A FIBER OPTIC DENSITOMETER. M.L.J. Landsman and G.A. Mook. Lab. of Chemical Physiology, Univ. of Groningen, the Netherlands.

The fiber optic densitometer differs from the oximeter described by Mook and Landsman (1) only in the light filters. For measuring indocyanine green two filter combinations are used 1.800 nm to measure the dye and 920 nm for compensation of non-specific effects and 2.800 nm and no filter in the compensating channel, a beam splitter replacing the dichroic mirror. The latter combination is about twice less sensitive for the dye, but about 4 times less sensitive for flow effects. With both filter combinations calibration lines obtained by recording the ratio of compensating over measuring photocell output at different dye concentrations is straight, at least up to 40 mg/1. Cardiac output determined in anaesthetized dogs from dye curves recorded from the pulmonary artery (PT) after injection into the inferior caval vein (IVC) has been found systematically lower than that determined from arterial dilution curves simultaneously recorded with a cuvette densitometer. Curves obtained from PT during continuous injection of dye into IVC show flow fluctuations with the respiration, from which in one experiment variations of 12% around the mean were found.

(1) Mook, G.A. and M.L.J. Landsman, Fiber optic reflection oximetry. Abstract, this congress, 1971.

Op-AVAILABILITY AND Op-CONSUMPTION OF THE BRAIN AFTER COMPLETE ISCHEMIA. <u>Etlang, R. Zimmer, G. Oberdörster</u>, Inst. f. Norm. u. Fath. Fhysiol, Cologne, Germany.

75 isolated perfused brains of dogs were subjected to complete ischemias of 1,5,10,20,30min duration in normothermia. Total cerebral venous outflow and venous 02-saturation were monitored continously. Ferfusion pressure was measured in the circle of Willis. Arterial 02-saturation, p02,pC02 and pH as well as brain temperature were kept constant.

Mean 02-availability was 8.1±1.4 ml/100g/min, mean 02-consumption 3.4±0.4 ml/100g/min.All ischemic periods were followed by an increase of 02-availability. The time until control values were reached was dependent on the duration of ischemia.Only after the shorter ischemias(1,5,10min)did venous 02-saturation return to control values at the same time as 02-availability. Immediately after these ischemias a temporary increase of 02-consumption was measured but a total repayment of the theoretical 02-debt was never observed. The calculated debt of 02-availability, however, was overpaid. The results show no consistent correlation between the post-ischemic 02-availability and 02-consumption. This may be explained by the irreversible cellular damage as well as a perivascular oedema impairing blood flow and

THE ROLE OF THE ALPHA RECEPTOR IN REGULATING NORADRENALINE OVERFLOW BY NERVE STIMULATION S. Z. Langer., E. Adler., M. A. Enero., F. J. E. Stefano. Instituto de Investigaciones Farmacológicas, Buenos Aires, ARGENTINA.

02-diffusion.

The noradrenaline (NA) stores in the isolated nictitating membrane of the cat and in guinea pig atria were labelled with dl-3H-NA. Transmitter overflow elicited by postganglionic nerve stimulation was determined by measuring the increase in outflow of 3H-NA and 3H-metabolites. Both phenoxybenzamine (PBA) and phentolamine increased the transmitter overflow induced by nerve stimulation. With the use of several concentrations of PBA "in vitro" as well as with different schedules of PBA pretreatment it was possible to dissociate the inhibition of the mechanisms of retention of released NA (neuronal and extraneuronal uptake) from the increased overflow in the presence of this agent. There was a coincidence between the concentrations of PBA required for alpha receptor blockade and those increasing overflow by stimulation. In isolated atria both phentolamine and tolazoline increased overflow of transmitter nearly 2 fold, while the increase in the presence of PBA was 5 fold. Since in atria the postganglionic receptors are mainly of the beta type, these results indicate that the increased overflow of NA in the presence of several alpha blocking agents could be due to a presynaptic effect.

These results are compatible with the presence of alpha receptors in adrenergic nerve endings playing a role in the regulation of transmitter output.

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994 ULTRASTRUCTURAL ASPECTS OF FAT MOBILIZATION FROM REPTILIAN ADIPOSE TISSUE IN RESPONSE TO ESTRONE. J. L. LaPointe. Dept. of Biology, New Mexico State University, Las Cruces, New Mexico, USA.

long progesterone/day for 10-20 days; 40ng estrone/day for 10-20 days and 14 hr light/day for 10-20 days respectively reduced peritoneal fat body weight to 38.2%, 8.6% and 37.2% of control values. Examination of the fat bodies of estrone-treated animals with the electron microscope revealed the development of a system of microtubules that appeared to be specifically associated with fat mobilization. The microtubules were 80Å in diameter with a lumen 30Å in diameter and up to 20 or more μ in length. They formed an orderly array around the lipid droplet and their ends penetrated the surface of the droplet. The microtubules were also in intimate contact with the nuclear envelope and the mitochondria. Pinocytotic vesicles were very numerous in these cells and "lipomicrons" 150Å in diameter appeared within the pinocytotic vesicles, in the intercellular fluid space and in the capillary lumina.

995 RESPONSES OF CEREBELLAR NEURONES TO ACTIVATION OF SPINOCEREBELLAR MOSSY FIBRE PATHS. B.Larson. Inst. of Physiology, University of Lund, Sweden.

Activation of the cutaneous component of the cuneocerebellar tract (CCT) evokes large mossy fibre field potentials in the cerebellar anterior lobe. In contrast activation of the group I component only evokes small negative fields in the granular layer (Körlin and Larson 1970). In the present experiments poststimulus histograms were taken from cerebellar neurones on their activation by volleys in the CCT and dorsal spinocerebellar tract (DSCT). The experiments were done on cats (decerebrate or chloralose) with spinal lesions for isolation of the CCT or DSCT. Muscle and skin nerves were stimulated electrically. In the CCT preparations poststimulus histograms were taken from 42 Purkinje cells of which 30 responded with increased or decreased 'single spike' firing rate after a latency of 6-10 msec. All of these cells responded to skin nerve stimulation but only five to stimulation of group I afferents and then usually weakly. Similar results were obtained in the DSCT preparations. Recordings were also made from presumed Golgi cells. These cells were usually activated on skin nerve stimulation with a similar latency as the Purkinje cells probably due to activation of the upper dendrites via parallel fibres. In addition some of these cells were monosynaptically activated from the mossy fibres. This early activation was highly specific, most cells responding to one nerve only. Three cells were activated by group I muscle afferents and two by cutaneous afferents.

THE EFFECT OF MUSCULAR ACTIVITY UPON OBESITY. S.B. Larsson. Inst. of Physiology, Odense University, Odense, Denmark.

Muscular activity in obese mice will cause reduction of the amount of fat in mice. Furthermore the lean mice will produce litters and the previous obese mice will also be fertile which is a cause of the muscular exercise. In goldthioglucose injected mice obesity will be prevented if the mice are exercised immediately after the injection.

MODIFICATION OF THE RAT FEEDING PATTERN AFTER REMOVAL OF OLFACTORY BULBS. C. Larue. Lab. de Physiologie des Sensibilités Chimiques et Régulations Alimentaires, Collège de France, Paris, France.

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The mean daily food intake of bulbectomised anosmic rats was approximatively unchanged. But, after operation, the day to day fluctuation of the daily intake was increased. Inside the diurnal cycle, the recorded feeding pattern: meal-size and meal-to-meal intervals were strikingly modified. Rats ate slowly scarced very long and large meals. This nibbling pattern was persistent in some rats for at least 20 days after operation. This altered feeding pattern was similar to that shown in recovered lateral hypothalamic rats. Conclusions are drawn in relation to the control of meal-size and of satiety mechanisms.

THE DIFFERENT CHARACTER OF EEG AROUSALS AND ASCENDING ACTIVATING INFLUENCES ON THE VISUAL CORTEX NEURONS OF RAT DURING THE ACTIVITIES OF HYPOTHALAMIC REWARDING ZONE AND OF MIDBRAIN FORMATION. L.P.Latash, B.M.Kovalzon, E.A.Kuman. The Grashchenkov Lab., USSR Academy of Sciences, Moscow, USSR.

In experiments with white rats a qualitative difference of two types of ascending activating influences probably realizing non-specific reinforcements of an opposite sign was revealed. 1/ In all the cases of EEG activation in the form of ngo-cortical desynchronization with hippocampal theta-rhythm (the orienting reaction with searching behaviour, REM sleep, self-stimulation or compulsory stimulation of lateral hypothalamic region) a regular rise of the cerebral cortex temperature was found, yet it was not observed when neocortical desynchronization appeared with hyppocampal one (spontaneously, the orienting reaction with animal's freezing, the fear reaction). 2/ The changes of the activity of the visual cortex neuron units (caused by flashes) during stimulations of the midbrain reticular formation and hypothalamic rewarding zone were of different character, as a rule. When differences were pronounced, the stimulation of the reticular formation increased short-latent and decreased long-latent components of neuron responses, whereas the stimulation of the rewarding zone gave a contrary effect.

THE BODY OXYGEN REGIMES REGULATION IN EARLY AGE. N.V.Lauer, M.M.Seredenko, M.M.Koganovskaya. Bogomoletz Inst.of Physiology, Ukrainian Academy of Sciences, Kiev, USSR.

The term "body oxygen regime" (OR) denotes certain interrelations of O₂ parameters (pO₂ and the quantities of O₂), ventilated in lungs, alveoli, transported by blood and consumed by tissues, and regulated by many physicological systems (N.V.Lauer, A.Z.Kolchinskaya). It was shown, that in relation to O₂ consumption the quantity of O₂, ventilated in lungs and alveoli under normoxia in early age, is equal of higher to some extent, while the arterial transport of O₂ under intensive metabolism in early age is almost the same as in adults. Satisfaction of higher O₂ demand than in adults is realised by depletion of O₂ reserves in mixed venous blood. The regulation of OR in early age under hypoxia is characterised by lower compensation of O₂ lack owing to insufficient increase of lung and alveolar ventilation, decrease of economicity and effectiveness of respiration, and abrupt diminution of O₂ parameters in arterial and mixed venous blood especially. The rising potentials of O₂ parameters regulators and increasing O₃ reserves in arterial and mixed venous blood in relation to body weight and O₃ consumption caused the increase in safety and firmness of the whole system of OR regulation in ontogeny.

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1000 RETINAL ADAPTATION AND S-POTENTIALS. M. Laufer, E. Essayag-Millán and H. Vanegas. Dept. Neurobiology, IVIC, Caracas, Venezuela

Three cone photopigments have been identified microspectrophotometrically

Three cone photopigments have been identified microspectrophotometrically in the teleost *E. plumieri*, with maximal absorptions at 471, 568 and 604 nm. Spectral sensitivity measurements of L-type S-potentials in photopic conditions reveal sensitivity maxima at 476, 568 and 606 nm. These results show a good correspondence between photopigment absorption and L-potential sensitivity, indicating the existence of independent transmission lines from the different varieties of cones, whose outputs do not mix at the receptor level. Under strict scotopic conditions, L-potentials with the same maxima are found when lights 1.5 to 3 log units above threshold are used, but at low levels of illumination slower potentials are recorded with sensitivity maxima at 500 nm, corresponding to rhodopsin absorption. A background light of 500 nm and 3 to 5 log units above threshold, falling upon the same receptor population as the test, produces a progressive shift of the 500 nm maximum to 568 or 606 nm, reversible after some minutes of darkness, depending upon duration and intensity of the background. These results indicate the existence of a rod-cone dual input to the units generating the potentials studied. When the background light is applied upon a different receptor population that the test, sensitivity shifts are also produced, indicating that a neural mechanism, not a photochemical one, is responsible for the shift. Pre- and post-adaptation dark potentials reveal no direct relation with spectral sensitivity changes.

1001 ELECTRON MICROSCOPE STUDIES OF GONADOTROPHS OF RAT PITUITARY AFTER INJECTION OF CRUDE HYPOTHALAMIC EXTRACT. Irene von Lawzewitsch. Centro de Investigaciones sobre Reproducción, Facultad de Medicina, Buenos Aires, ARGENTINA.

The electron microscope features of rat gonadotroph cells (FSH and LH) after the intracarotid injection of 100 mg crude hypothalamic extracts were compared with those of somatotrophs and mammotrophs of the same glands. The animals were sacrificed by decapitation 5,10,20,30,60,90 min and two days after injection. Control animals were sacrificed according to the same schedule. Tissue fragments were fixed in 2% glutaraldehyde cacodylate-buffer, refixed in buffered osmium tetroxide and embedded in maraglas. A marked extrusion of granules into the perivascular spaces from somatotrophs and LH-cells was already observed after 5 to 10 min; from mammotrophs and FSH-cells after 10 to 20 min. The secretory granule contents of pituitary cells decrease until 30 min after injection, but at that moment we can observe a very active Golgi apparatus, and a prominent endoplasmatic reticulum as well as pinocytose activity. The releasing phenomenon was present in almost all of the cells, while the contents of mature granules increased and cellular hypertrophy was seen.

The morphological findings observed in all pituitary cells correspond to the action of nonpurified hypothalamic extracts.

DATA ON THE BIOLOGICAL EFFECTS OF SYNTHETIC POLY-GLUTANIC DERIVATIVES.

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Sch. Med., Szeged; Inst. of Organic Chemistry, Eötvös Loránd Univ.,

Pudapest and Inst. of Organic Chemistry, József Attila Univ., Szeged,

Hungary

According to our investigations poly-DMAG 94 Glu causes carbon retention in the pulmonary and glomerular capillaries while the clearance of carbon from the blood stream is significantly accelerated examined by the method of Biozzi et al./1953/. This synthetic poly-glutamic derivative causes also a decrease of the blood fibrinogen level, that of thrombocyte count and a significant leukocytosis. In higher doses this compound leads to afibrinogenemia primarily due to intravascular defibrination followed by secondary fibrinolysis. Py fluorescein-antifibrin serum fibrin was demonstrated in the glomerular capillaries and fibrinogen-fibrin degradation products were present in the serum, latter could be inhibited by the administration of EACA. All the effects of poly-glutamic derivatives mentioned above are connected with their basic character, since the decrease of that results in the weakening of these effects.

THE HEAT OF SHORTENING IN THE WHOLE CONTRACTION-RELAXATION CYCLE OF STRIATED MUSCLE. J. Lebacq and X. Aubert. Dept de Physiologie, Univ. of Louvain, Louvain, Belgium.

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The net thermal effect of shortening on the heat production of normal and dinitro-fluorobenzene (DNFB)-poisoned Sartorius muscle of Rana temporaria has been analyzed at 0°C up to the end of relaxation, in the following conditions: tetani with rapid shortening at constant velocity during the plateau of tetanic activity and with subsequent redevelopment of tension and isometric tetani at the two extreme lengths of the movement. In these conditions, shortening heat appears clearly and 75-85 % of it persist up to the end of relaxation. This effect is not reduced by DNFB. The reduction, occuring during relaxation, of the initial effect of shortening, is fully accounted for by the fact that the tension redeveloped after the end of the movement remains always below the tension developed in a tetanus at the same final length, but isometric from the start. Shortening heat can thus not be part of a cyclic process reversed during relaxation; it must involve the expenditure of free energy.

LITHIUM UPTAKE BY ISOLATED EPITHELIUM FROM FROG SKIN AND ITS INHIBITION BY AMILORIDE. G. Leblanc and R. Lemonnier. Dept. de Biologie, CEN-Saclay,91 Gif/Yvette, FRANCE.

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Intracellular L1 content of isolated frog skin epithelia exposed to different Na-free Li-containing external solutions under short circuit conditions, was determined by flame photometry. Internal bathing media was always conventional Na Ringer. Once equilibrated with normal Ringer solution, the external side of the epithelium was briefly rinced with Choline solution and then exposed to Li media for 30 to 50 min. In this conditions, epithelial cells accumulate Li ions: when external Li concentrations were 1, 2.5, 10 and 25 mM/l., intracellular Li amounted to 9, 16, 20 and 28 mM/l. of cell water respectively. However, epithelia pretreated externally with Amiloride (5 10-4 M.) exhibited lower cellular Li content values than the corresponding external Li concentrations, and did not exceed 2 mM/l. of cell water when outside Li was either 10 or 25 mMolar. The addition of 25 mM/l. of Na to the external bath containing 2.5 mM/l. of Li drastically reduced Li uptake, whereas the same amount of K had no effect. The Li uptake results are difficult to explain in terms of an entirely passive Li movement across the external border of the frog skin epithelium, since it would require an intracellular potential 50 mv negative with respect to the external bath when the lowest Li concentrations are used.

ELECTROPHYSIOLOGICAL EVIDENCE FOR A PRESYNAPTIC ACTION OF A GANGLION-BLOCKING AGENT. G. M. Lees and S. Nishi. Dept. of Pharmacology and Therapeutics, Loyola Univ. Med. Ctr., Maywood, Ill., U.S.A.

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Intracellular recordings were made of responses to orthodromic stimulation of cells in rabbit isolated superior cervical ganglia. Possible presynaptic actions of ganglion-blocking drugs were investigated on post-tetanic potentiation (PTP). Conditioning trains of stimuli were delivered at a frequency of 10-40 Hz for 10 s. Before and after the conditioning stimulation, test stimuli were given at a frequency of 0.3 or 0.5 Hz. Mecamylamine (10 -10 M) reduced the amplitude of EPSPs but had no effect on action potentials evoked by antidromic or direct stimulation of the cell and no consistent effect on the membrane resting potential. PTP was abolished by mecamylamine; the time-course of inhibition and recovery of PTP followed closely the time-course of the effect of mecamylamine on the amplitude of EPSPs. In concentrations which greatly reduced the amplitude of EPSPs, hexamethonium, pempidine, tetraethylammonium and (+)-tubocurarine did not inhibit PTP. It is concluded that inhibition of PTP is not an essential feature of the ganglion-blocking action of these drugs. Mecamylamine, however, acts both pre- and post-synaptically in concentrations which inhibit ganglionic transmission. Supported by National Science Foundation Grant GB-8718

1006 POSITIVE FEEDBACK ACTIONS OF A MYOCARDIAL DEPRESSANT FACTOR IN THE PATHOGENESIS OF CIRCULATORY SHOCK. Allan M. Lefer. Dept. of Physiology, Univ. of Virginia School of Medicine, Charlottesville, Virginia, U.S.A.

A myocardial depressant factor (MDF) has been isolated from the plasma of cats, dogs, and humans in a variety of forms of circulatory shock including hemorrhagic, endotoxic, cardiogenic, bowel ischemic and pancreatitis shock. MDF has been identified as a peptide having a molecular weight of 800 to 1000 and appears to be formed by the hydrolytic action of lysosomal proteases which originate in the ischemic pancreas. Agents which stabilize lysosomal membranes (e.g., high doses of glucocorticoids), and protease inhibitors (e.g., aprotinin) administered early in the course of shock, prevent the appearance of MDF and prolong survival 3-4 fold. MDF exerts a marked negative inotropic effect in the isolated or in situ heart (independent of changes in heart rate, preload, or coronary flow) paralleling its concentration in the plasma. MDF also appears to enhance depression of phagocytic function in the reticuloendothelial system but not in leukocytes during shock. Furthermore, MDF exerts a constrictor effect on splanchnic resistance vessels both in the presence and absence of catecholamines. The following sequence of events occurs in hemorrhagic (and other forms of) shock: hypotension \rightarrow splanchnic vasoconstriction \rightarrow acidosis \rightarrow splanchnic ischemia \rightarrow release of lysosomal acid proteases \rightarrow formation of MDF \rightarrow myocardial depression + enhanced splanchnic ischemia + enhanced RE depression. Thus MDF, in addition to depressing the myocardium, retards its own removal and/or inactivation and generates additional MDF.

1007 EXTRACTION OF OXYGEN FROM AIR IN HYPOXIC AND NORMOXIC SUBJECTS. R. Lefrançois, P. Pasquis, H. Gautier, A.M. Ceväer and J. Leroy. Lab. Physiol., Hôtel-Dieu, 76 - Rouen, France.

Extraction coefficient of oxygen (E), as defined by Dejours, Garey and Rahn (1970), is unaffected by changes in barometric pressure. Thus, calculation of E must be important for the comparison of gas exchanges in sea-level subjects and high altitude natives. It has been determined at sea-level for two levels of oxygenation and at the elevation of 3660 m, in highlanders and acclimatized lowlanders, at rest and during exertion. 1°) For all subjects, in all conditions, for increasing loads of exercise, E increases and is maximal for a load of 120 watts. 2°) Resting and exhaution values are not different. 3°) At 3660 m, the values of E, at any load, are higher in highlanders than in lowlanders. Former subjects are able to extract more oxygen of a given air flow. 4°) For lowlanders, E is not different in acute and chronic hypoxia but higher than in normoxia. The determination of E can be used to appreciate the degree of altitude acclimatization.

MICROPUNCTURE STUDIES OF MAGNESIUM TUBULAR REABSORPTION IN RATS. Le Grimellec, Ch., Roinel, N., Morel, F., Dept. of Biol., Centre d'Etudes Nucléaires, Saclay, France.

Micropuncture experiments to ascertain magnesium excretion were performed on 5 rats during antidiuresis and subsequent i.v. Mg loading, using the recollection technique. Magnesium concentration in samples of tubular fluid, final urine and plasma ultrafiltrate (P_f) was determined by electron microprobe analysis. During antidiuresis (P_f = 0,50mM), low Mg fractional reabsorption was observed in the proximal convoluted tubule [(TF/P)In = 2,21 \pm 0,08; (TF/P_f)Mg = 1,90 \pm 0,08; (TF/P)Mg/In = 0,86, N = 31] . A significant correlation (r = 0,72) was found between (TF/P_f)Mg and (TF/P)In. The results for distal samples [(TF/P)In = 4,47 \pm 0,2; (TF/P_f)Mg = 0,63 \pm 0,06; (TF/PMg/In = 0,14, N = 20] indicate that most of the filtered magnesium was reabsorbed in the loop of Henle, and that there may have been additional reabsorption in the collecting duct (CMg/CIn = 0,08, N = 10). Under Mg loading (P_f = 1,07 mM), fractional reabsorption in the proximal tubule remained nearly constant [(TF/P)Mg/In = 0,81, N = 35] . Distal values [(TF/P_f)Mg = 1,33 \pm 0,08, (Tf/P)Mg/In = 0,37, N = 28] indicate a drop in Mg fractional reabsorption along the loop, suggesting that Mg reabsorption in this segment is a saturable process. Under these conditions, urinary Mg excretion increased greatly (CMg/CIn = 0,56, N = 10); this value suggests a net addition of Mg along the collecting duct.

SCALP FIELD DISTRIBUTION OF HUMAN ALPHA EEG.

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D. Lehmann. Dept. of Neurology, Univ. of Zürich, Switzerland. The topographical distribution of the electrical fields on the human scalp during relaxation (alpha EEG) were studied with a 48-channel recording system. The data were displayed as series of equipotential maps. The field distributions were relatively simple, and therefore, they could be characterized by the locations of their maximum values (positive and negative). These maximum values were found preferentially in a circumscribed region consisting of a pre-vertex to parietal midline area, a left occipital, and a right occipital area. The difference of occurrence of the field maxima in preferred and non-preferred regions was significant (p $\langle 0.005\rangle$) for the subject population. The preferred regions were very similar between subjects. - Such data on the distribution of the electrical fields on the head may be used to model the human EEG. It seems that the assumption of three generators will account for the main properties of the observed alpha fields.

SYMPATHETIC REGULATION OF FLUID BALANCE AND FOOD INTAKE BY RECIPROCAL ACTIVITY OF α- AND β-ADRENERGICALLY CODED HYPOTHALAMIC CENTERS. David Lehr and Warren Goldman. Dept. Pharmacol., N.Y.Med. Coll., Flower & Fifth Ave. Hosps., New York City, U.S.A.

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In our earlier work (Lehr, et al., The Pharmacologist 8: 190, 1966; 10: 180, 1968; J. Pharmacol. & Exptl. Therap. 158: 150, 1967), it was shown that isoproterenol (Iso), a β-adrenergic agonist, injected s.c., evoked copious drinking and simultaneous antidiuresis in water sated rats, whereas, metaraminol, an a-adrenergic stimulant, produced sustained diuresis and concomitant suppression of drinking in thirsty rats. Food consumption in the hungry rat was sharply reduced by Iso, indicating that adrenergic stimulation of eating was controlled by a-adrenergically coded neurons only. The existence of central adrenergic mechanisms of food and water regulation, in which a- and β-coded neurons (hunger and satiety centers) mediate reciprocal effects, was postulated. The correctness of this hypothesis was established in brain cannulated rats (Leibowitz, Nature 226: 963, 1970; Goldman and Lehr, Nature, under publication). The actions of serotonin (5-HT), given peripherally or centrally, were closely similar to those of Iso upon both drinking and eating, including inhibition by β-adrenergic blockade (Goldman and Lehr, Fed. Proc., 1971, in press). In contrast to Iso and 5-HT, appetite suppression induced by peripheral administration of amphetamine was found not to be mediated by the β-adrenergic satiety center. (Supported by grant HE-00890-19 of the NIH, NHI, U.S. Public Health Service and the Hoffman-LaRoche Foundation).

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BARBITURATE SPINDLES AND RECRUITING RESPONSES IN MOTOR CORTEX AND PYRAMIDAL TRACT IN THE CAT. I. Lehtinen, Dept. of Physiology, Univ. of Turku, Turku, Finland.

Barbiturate spindles, tripped spindles and recruiting responses were transcortically recorded from several points of the cerebral cortex in the cat. Slow wave activity with accompanying multi-unit discharges was simultaneously recorded from the medullary pyramidal tract. Bipolar stimulating electrodes were inserted into the nonspecific thalamus to elicit tripped spindles and recruiting responses in the motor cortex and pyramidal tract. Studies showed that both barbiturate spindles and recruiting responses usually occur simultaneously at several points of the motor cortex in the same hemisphere, but a marked asynchrony is found when the comparison is made with the corresponding recording points of the contralateral hemisphere or with the ipsilateral recording points in the marginal and suprasylvian gyri. The slow waves, with accompanying multi-unit discharges, recorded from the pyramidal tract usually occurred in phase with the barbiturate spindle waves, tripped spindle waves and recruiting responses recorded from the lateral end of the ipsilateral cruciate sulcus. The data show that asynchrony of these rhythmic activities between the hemispheres also manifests itself in the function of the pyramidal tracts and perhaps in the target neurons of the tract. (Supported by The Finnish Medical Fndm.) 1012 FAT SYNTHESIS-FAT MOBILIZATION DIURNAL CYCLE IN RATS AS AN UNDERLYING ME-CHANISM IN THE REGULATION OF FOOD INTAKE AND BODY WEIGHT. J. Le Magnen. Lab. de Physiologie des Sensibilités Chimiques et Régulations Alimentaires, Collège de France, Paris, France.

It has been shown by the simultaneous recording of respiratory exchanges and of feeding patterns in rats that the rate of energy intake was much higher at night and much lower in day time than the concommitant energy output (0, consumption). High values of respiratory quotient at night and low values in day time indicated that the excess of calories eaten in the dark period was stored as fats, and these fats mobilized in the light period to compensate for the deficient intake in this period. Some indications were given by these results on the relationship of lipostatic and glucostatic mechanisms to the control of food intake and on its role in the regulation of body weight. New experimental data presented here, particularly on the occurrence of a diurnal cycle of P.F.F.A. concentration and of insulinosecretion support and extend the previous conclusions.

ANALYSIS OF ELEMENTARY ACTIVITY OF THE CARDIAC PACEMAKER. J. Lenfant, J. Mironneau and Y. M. Gargoufl. Lab. of Animal Physiology, CNRS-ERA, n°111, 86 - Poitiers, FRANCE.

The electrical activity of the rabbit heart is recorded by means of microelectrodes. Selective inhibitors and modifications of external ionic solutions are used for the study of the auricle and sino-auricular node responses. Tetrodotoxin, an inhibitor of the rapid initial sodium permeability, suppresses the auricular response but does not modify the sinusal activity. Manganese chloride, an inhibitor of the slow inward current, depresses the sinusal activity while the auricle can always show responses but without plateau. Lanthane chloride, which blocks membrane calcium fluxes, slightly acts on the pacemaker responses. The spontaneous activity is suppressed in a sodium-free solution but slightly modified in a calcium-low solution. These results suggest that a slow inward current, essentially carried by sodium ions, may be involved in the keeping of the cardiac pacemaker activity.

1014 RELATION BETWEEN MECHANICAL ACTIVITIES AND IONIC CURRENTS IN FROG ATRIAL TRABECULAE AND RAT VENTRICULAR FIBERS. C. Léoty, G. Raymond and Y.M. Gargouîl. Laboratory of Animal Physiology, CNRS, ERA 111, 86-Poitiers, FRANCE.

A microphotometric method was combined with the double sucrose gap technique to permit the tension measurement on the small membrane area (diameter : 20 to 40 μ ; length:80 to 100 μ) where the voltage or current records were obtained in frog atrial trabeculae and rat ventricular fibers. In frog, when the depolarizing pulse duration was longer than 100 ms, the contractile response shown two components : the first was $I_{\rm Ca}$ dependent while the second was only outward current dependent. In rat only the first component was observed. These results could be reported to morphological differences between these two myocardial tissues but also to the presence or absence of membrane delayed rectification.

CORRELATIONS BETWEEN THE VENTRICULAR GRADIENT (QRST AREA) AND THE MYO_CARDIAL GRADIENTS OF K, Na, Ca AND Mg. <u>E. Lepeschkin</u>, <u>H. Kimura</u> and <u>W</u>. Raab. Dept. of Med., Univ. of Vermont Col. of Med., Burlington, Vt. U.S.A.

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In 56 patients dying from various cardiac and non-cardiac causes the concentration of K, Na, Ca and Mg were determined in myocardial samples from the lateral wall of the right ventricle, the right and left halves of the septum, and the endocardial and epicardial regions in the apical and basal lateral wall of the left ventricle. The QRST area (AQRST) in lead aVL was correlated with the left transmural electrolyte gradients at the base, that in lead V5 with those at the apex, and that in lead V3 with those between right ventricle and septum. A good positive correlation was obtained between AQRST and the K, Mg and especially K/Na gradients, a negative correlation between AQRST and the Na and Ca gradients. A less distinct positive correlation was found between the apico-basal K/Na gradient and AQRST in leads II and V5. In view of previous studies on the effect of K, Na, Ca and Mg on myocardial repolarization mechanisms are discussed whereby myocardial electrolyte gradients could be responsible in part for the normal and abnormal ventricular gradient.

DIE BEZIEHUNG ZWISCHEN DER GASTRISCHEN SEKRETIONSDYNAMIK UND DEM EXPERIMENTALEM MECHANISCHEM IKTERUS. Gh.Leporda, S.Dolinescu, S.Freund, R.Leporda. Inst.für Öffentliches Gesundheitswesen und Medizinische Forschung Jassy, Rumänien.

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Zusammenfassung. (1) Im Laufe des Studiums der gastrischen dynamischen Sekretion mit kleinem Pavlov-schen Magen bei Hunden, in Zeiträumen von je 12 Tagen, während des experimentellen mechanischen Ikterus, nach der Wiederherstellung des Gallenflusses und nach der intravenösen Galleverabreichung haben die Verfasser festgestellt, daß: (2) Während des experimentellen mechanischen Ikterus, durch Ligatur des Koledokes, die gastrische Sekretion stark ansteigt, und daß sie während der ganzen Zeit des Gallenhindernisses anhält. (3) Nach der Wiederherstellung des Gallenflusses sinkt die gastrische Sekretion sofort, und nach der Koledokoduodenostomie erreicht sie das physiologische Niveau. (4) Nach der intravenösen Verabreichung von Galle sinkt die gastrische Sekretion bis zu Null in Form eines Gefälles. (5) Das Ansteigen der sekretorischen Activität während der billaren Stase durch das koledoktische Hindernis ist der iritierenden Wirkung der Interzeptoren des Koledoktes und nicht den zusätzlichen inflamatorischen Faktoren der Erweiterung des Kolezistes oder dem Eindringen der Salze und Pigmente ins Blut zuzuschreiben.

EFFECT OF ACUTE COLD EXPOSURE ON BLOOD TSH AND CORTICOSTERONE CONCENTRATIONS IN THE RABBIT. J. Leppäluoto, H. Lybeck and P. Virkkunen. Inst. of Physiology, Univ. of Helsinki, Finland.

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In adult man the serum TSH level does not alter during acute cold exposure. But increased TSH levels have been consistently reported in the rat. An explanation for the unaltered serum TSH level is probably the stress-induced secretion of ACTH, which could inhibit the coincident secretion of TSH. The secretion of TSH and ACTH were therefore studied during acute cold exposure. Intact and dexamethasone-pretreated animals (20 rabbits) were exposed to mild and severe cold for 2 hr. Blood TSH was measured by McKenzie bioassay and ACTH by fluorometric assay of corti-When intact animals were exposed to mild or severe cold, no costerone. increase of blood TSH could be detected, whereas the corticosterone level rose maximally. When dexamethasone-pretreated animals were exposed to mild cold, TSH and corticosterone levels were unchanged, and when they were exposed to severe cold, the TSH level was again unchanged, but the corticosterone level was moderately increased. It appears that acute exposure to cold does not induce the pituitary cells to secrete TSH. Evidently, during exposure to severe cold, they prefer to secrete ACTH, in spite of dexamethasone pretreatment.

1018 ESTIMATION OF QUANTAL CONTENT IN DETUBULATED NERVE-MUSCLE PREPARATION. Halina Lermer Dept. Physiol. Heb. Univ. Med. Sch., Jerusalem, Israel.

Osmotic shock with hyperosmotic glycerol-Ringer disrupts the transverse tubular system in muscle and abolishes contractions (Howell & Jenden; Fed. Proc. <u>26</u>: 553, 1967). In this detubulated preparation neuromuscular transmission is practically unimpaired and end plate potentials (e.p.p.s), miniatures e.p.p.s (m.e.p.p.s) and reversal potentials can be measured. Thus different estimates of the quantal content (m) can be compared; m₁ (= e.p.p./m.e.p.p.) is an underestimate of the 'true' value of m, m₂ (estimated from the fluctuations in e.p.p. amplitude) is an overestimate of m. The Katz- Martin equation (m= 3 m₁ 2 m₂) (Martin; Physiol. Rev. <u>46</u>; 51, 1966) was tested experimentally in this detubulated preparation. It was found that the values of m obtained after correction for the driving force, fit the values derived from the Katz- Martin equation.

1019 HEMATOLOGIC EFFECTS OF SYNTHETIC ATMOSPHERES. M. A. Lessler, H. S. Weiss, and C. E. Hendrich. Dept. of Physiology, Ohio State Univ., Columbus, Ohio, USA, 43210

One of the main reasons for replacing air in sealed cabin environments is the increased load of the vehicle due to the presence of nitrogen, and the problems of solubility of nitrogen in the body fluids. We tested the effect of exposure of 200 gram rats (initial weight) to atmospheres in which the partial pressure of oxygen was 565, 380, or 195 mm Hg with nitrogen, helium, or neon as the diluent gas. The rats were maintained at atmospheric pressure in isolators in which the synthetic atmospheres were maintained at controlled temperature, humidity and carbon dioxide content. Animals were removed through locks after 10, 20, or 30 days of exposure and hematocrit, RBC count, RBC fragility, hemoglobin concentration, and blood volume was determined. When these data were compared to pair fed and full fed controls maintained in air, it was evident that changes in hematology had occurred. The changes were greatest in oxygen when no diluent gas was used, and least when nitrogen was the diluting gas. The effects were intermediate for helium and neon. Hematologic changes were most evident during the first 10 day period, and tended to approach control values by 30 days.

DISSOCIATION OF ABSOLUTE NET REABSORPTIVE RATES FOR WATER AND BICARBONATE (CH2O, CHCO3) OF RAT PROXIMAL TUBULES IN METABOLIC AND RESPIRATORY ACIDOSIS D.Z. Levine, L.A. Nash and J. Lemke. Department of Medicine, University of Ottawa, Ottawa, Canada.

Recent studies on isolated perfused rabbit proximal tubules and doubly perfused rat proximal tubules postulate H⁺ secretion significantly influences CH₂O. Since CHCO₃ also depends on H⁺ secretion, this hypothesis would predict parallel changes in CH₂O and CHCO₃. To evaluate this under in vivo free-flow conditions, recollection micropuncture (10 rats, 45 tubules) was done in normocapnia (control) and acute hypercapnia(pCO₂= 120 mmHg) in HCO₃-loaded rats; and in chronic NH₄Cl acidosis (plasma HCO₃=14 mEq/l) compared with its acute correction (plasma HCO₃=28 mEq/l). TF HCO₃ was measured with a glass micro-pH electrode. In hypercapnia, SNGFR and TF/P inulin were unchanged while TF/P HCO₃ fell (p<0.00l). Although CH₂O was constant, CHCO₃ rose from 1197±180 (control) to 1576±209 puEq/min., p<0.01. After correction of NH₄Cl acidosis, SNGFR and TF/P HCO₃ rose (p<0.01) and TF/P inulin fell (p<0.001). Divergent changes in CH₂O and CHCO₃ resulted in a marked increase in the ratio: CHCO₃/CH₂O. In NH₄Cl acidosis CHCO₃/CH₂O was 47.6±2.5 and increased to 74.2±9.4 puEq/nl after correction, p<0.05. Conclusion: the control of CH₂O is not principally mediated by H⁺ secretion during the above acute acid-base changes.

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DIRECT MEASUREMENT OF TENSION WITHIN LEFT VENTRICULAR WALL OF THE DOG HEART. B.Lewartowski and G.Sędek. Dept.of Clinical Physiology, Postgraduate Medical Education Center, Warsaw, Poland.

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Latitudinal and longitudinal tension was directly measured with the strain-gauge transducer coupled to the left ventricular wall by means of two pairs of stiff pins. The forces developed by the muscular segment between the legs of transducer were eliminated by reducing the distance between the pairs of pins after they have been inserted. Therefore the only force measured was the wall tension. It has been found, that latitudinal tension attains its maximum at the end of isovolumetric contraction / stress calculated from tension and wall thickness = 96 - 15 G/cm² /, whereas longitudinal tension is at the same moment by 40% less. In the isotonic phase latitudinal tension falls despite the growing ventricular pressure, whereas longitudinal tension continues to increase at a smaller rate. The direct measurements of stress are in good agreement with results of calculations of stress from linear dimensions of the heart and ventricular pressure substituted into the published formulas.

THE LAYERING-SEQUENTIAL VENTILATION PROBLEM STUDIED BY MEASURING THE COMPOSITION OF RESIDUAL AIR. Benjamin M. Lewis. Wayne State Univ. Sch. of Med. Detroit, Mich. USA

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The composition of an inspired foreign gas falls continuously during the following expiration. If this is due to layering of the inspirate on top of the gas present in the lungs, the terminal expirate will have a higher concentration of the test gas than the residual volume. If the fall is due to early emptying of a region of high concentration and the late emptying of a region of low concentration the residual volume, being a mixture of the two, will have a higher concentration of the test gas than the terminal ex-The composition of residual air was measured by introducing boluses of helium or hydrogen, measuring the amount of the test gas expired and, by difference, the amount retained while simultaneously determining the residual volume in which it was retained by a double gas dilution technique of high accuracy. In 11 studies in 10 normal subjects the boluses were introduced during a vital capacity maneuver. In 9 concentration of the test gas was higher in the residual volume than in the terminal expirate, but in only 2 of 6 studies in which boluses were introduced during a 1000 ml breath taken from FRC was this found. However, in all 3 studies in which boluses were introduced during a 1000 ml breath taken near VC residual volume concentration exceeded that in the terminal expirate. These data indicate that when the breath is deep sequential ventilation is chiefly responsible for the changing composition of the expirate, while layering contributes to this phenomenon after a shallow tidal breath.

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LOCAL REGULATORY FACTORS AND SKELETAL MUSCLE BLOOD FLOW IMMEDIATELY AFTER TRAUMA. D.H. Lewis, J. Nolte, J. Sandegård, L. Fondberg and T. Seeman. Dept. Surgery I and II, Univ. Göteborg, Göteborg, Sweden.

Trauma to skeletal muscle increases transiently non-nutritional flow through the injured tissue. Purpose of present study was to investigate role of local biochemical changes in flow regulation in trauma, including inhibition of vasoactive kinins. 15 dogs were anesthetized i.v. with Na pentobarbital and catheters placed in jugular v., iliac art., iliac vein bilat, and carotid art. Flow in iliac art. and v. were measured with square-wave flowmeter. Trauma was 200 blows to each thigh with padded hammer. 7 dogs were given Trasylol (200,000U then 2000U/kg/hr. Trauma increased local flow transiently. Local venous samples showed immed. and sustained increase in pO2,pCO2 and lactate and decrease in pH. Osmotic press. increased usually immed. but occas. after 15-30 min. K increased immed. then returned towards but not to control. Na was unchanged and Hct fell slightly. Pattern of flow response was not altered by Trasylol given 30 min after trauma, but was poss. less increased with Trasylol before trauma. Trasylol alone had no effect on parameters studied. Results are not in keeping with idea that osmotic press. or electrolytes are responsible for flow changes after trauma but leave open question as to role of vasoactive kinins.

DOPAMINERGIĆ SYNAPTIC ACTIONS IN SYMPATHETIC GANGLIA. Benjamin Libet and Tsuneo Tosaka.

Dept. of Physiology, Univ. California, Sch. Med., San Francisco, California, U.S.A.

Dopamine (DA) apparently mediates two synaptic actions in superior cervical of rabbit: (1) DA is a transmitter for the slow inhibitory postsynaptic potential (S-IPSP); (2) DA facilitates selectively the slow excitatory PSP response (S-EPSP, itself mediated directly by muscarinic action of acetylcholine, ACh). DA is presumably released by preganglionic ACh (muscarinic) excitation of DA-interneurons. The direct need of a second non-ACh transmitter for S-IPSP is seen in the abolition by low Ca/Mg of the hyperpolarizing but not the depolarizing response of ganglion cells to muscarinic agents. Both slow PSP's are depressed by some alpha blockers (e.g. phenoxybenzamine); both are augmented by blockade of dopamine oxidase (by diethyldithiocarbamate) and by COMT inhibitors (e.g. tropolone; the latter indicates that inactivation of catecholamine by catechol-0-methyl-transferase can be a factor in limiting these slow PSP's). Prolonged muscarinic action (by bethanechol) abolishes S-IPSP and depresses S-EPSP, presumably by depleting DA stores; re-uptake of extrinsic DA can restore both responses (norepi- and epinephrine are relatively ineffective). Action (2) of DA has added unique characteristics: It occurs with an amount of DA too little to elicit any PSP itself; it endures for hours; phenoxybenzamine can block it before but not after its initiation; norepi- and epinephrine are relatively ineffective. Action (2) appears to involve an enduring postsynaptic change produced by one synaptic transmitter (DA) in the metabolic or structural features that affect the electrogenic response (S-EPSP) to another transmitter (ACh, acting muscarinically). (Supported by USPHS, NIH Grant NS-00884.)

WATER AND SODIUM EXCRETION FOLLOWING BLOOD VOLUME EXPANSION UNDER CONDITIONS OF CONSTANT ARTERIAL, VENOUS AND PLASMA ONCOTIC PRESSURES AND CONSTANT HAEMATOCRIT. B.Lichardus and A.Nizet.Inst.Exper.Endocrinology, SAV, Bratislava, CSSR and Inst.Med., Univ. of Liège, Liège, Belgium.

In 12 anesthetized dogs the left kidney was tied off and another kidney from donor dogs was transplanted to the neck. In the latter the arterial pressure was kept constant by using a screw-clamp and the venous pressure by tilting the animal. Blood volume was expanded by transfusing homologous blood with the haematocrit and oncotic pressure adjusted to match the values found in the recipient dog. Exogenous ADH and DOCA were administered. Functional behaviour of the transplanted kidney before the expansion was normal and comparable to the right kidney in situ. Diuresis and natriuresis following the expansion due to the increased GFR and/or to the decreased tubular reabsorbtion was more pronounced in the kidney in situ with uncontrolled perfusion pressure. As changes of the filtered fraction were unavoidable following expansion in both kidneys the increased peritubular plasma oncotic pressure could have counteracted a possible more specific humoral natriuretic effect in the transplanted kidney. The increase of renal perfussion pressure in the kidney in situ opposing the antinatriuretic effect of the peritubular plasma oncotic pressure appears to be the decisive non-humoral natriuretic factor during blood volume expansion.

REPONSES VISUELLES UNITAIRES CHEZ LA TRUITE. B.LIEGE et G.GALAND. Lab. Neurophysiologie, Faculté Sciences, Poitiers, France.

1) Au niveau des cellules ganglionnaires on rencontre principalement : unités on ; unités off, certaines étant directionnelles ; unités on-off directionnelles ou non ; unités spontanées ; certaines unités sont en activité permanente, leur fréquence de décharge variant soit en sens inverse, soit en sens direct de la luminosité ambiante, faisant ainsi penser aux unités de la classe 5 et à certaines unités de la classe 3 déjà décrites chez la Grenouille. 2) Dans le tectum et le mésencéphale profond : unités de nouvauté ; unités de similitude ; unités spontanées. 3) Dans le reste du système nerveux central (télencéphale, diencéphale, mésencéphale ventral et métencéphale) on rencontre des unités très différentes : grand champs, réponses aux mouvements et à la stimulation on-off générale ; les phénomènes d'habituation sont très fréquents. Certaines de ces unités sont binoculaires ; d'autres présentent des phénomènes de convergence heterosensorielle : ces unités répondent à la fois à la stimulation visuelle et à la stimulation électrique des téguments au niveau de la ligne latérale (ipsi ou contralatérale). Ces résultats montrent que les phénomènes de convergence hétérosensorielle à composante visuelle sont largement distribués dans le système nerveux central de la truite. Toute laisse penser qu'ils devraient conduire à une meilleure interprétation des processus d'intégration visuelle siégeant au dela de la voie visuelle primaire.

EXPIRATORY PO AND PCO CURVES IN NITROGEN, HELIUM, AND ARGON. W.Liese, U. Smidt, P.Lotz, K.Muysers. Inst.of Physiology, Univ.of Bonn, Bonn, German Fed.Rep.

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To investigate intrapulmonary gas mixing the expiratory p0, and pC0, curves have been followed simultaneously and continuously by mass spectrometry in 10 subjects. The curves have been plotted against tidal volume during breathing of the following gas mixtures: nitrogen 79%-oxygen 21%, helium 79%-oxygen 21%, and argon 79%-oxygen 21%. The mean volume of gas expired for a decrease in p0, from 75% to 25% of the final amplitude was 81.6 ml for N₂/O₂, 66.1 ml for He/O₂, and 71.9 ml for Ar/O₂. The respective figures for CO₂ are 84.9 ml, 68,5 ml, and 80.6 ml. During expiration of the last 300 ml of the tidal volume the mean decrease in pO₂ was 4.7 torr for N₂/O₂, 3.4 torr for He/O₂, and 6.8 torr for Ar/O₂. The simultaneous increase in pCO₂ was 2.8 torr for N₂/O₂, 2.1 torr for He/O₂, and 3.7 torr for Ar/O₂.— The differences in the volumes of gas expired for a given change in partial pressure may be attributed to variations in diffusion and streaming in the central parts of the lung, whereas the differences in the alveolar plateaus of the partial pressure curves can be explained by diffusion in the peripheral parts of the lung and by the shape of the dissociation curves of O₂ and CO₂.

GLANDULAR COMPONENTS OF FROG SKIN CATECHOLAMINE RESPONSE. B.D. Lindley. Dept. of Physiology, Case Western Reserve University, Med. Sch., Cleveland, Ohio 44106.

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The whole surviving skin responds to stimulation by epinephrine or norepinephrine with increased short-circuit current. The conductance usually increases, but may show an initial decrease in belly skin with few granular glands. Isolated epidermis of skin split by trypsin treatment and gentle dissection has mucous glands still attached, whilst granular glands are left in the corium. Isolated epidermis responds to E and NE with small decreases or no change in conductance and with small decreases in short-circuit current. Single mucous glands were studied with microelectrodes in both split and whole skin. The lumen is 10 mV negative to the corium surface, and the glands respond to E and NE with graded reversal of p.d., reaching 30 mV change. This response corresponds to a decrease in skin short-circuit current. Single granular glands, normally lumen-negative, show depolarization upon stimulation. The whole skin conductance increase is largest in areas with most numerous granular glands. The conductance increase reflects the granular gland response and that the short-circuit current increase depends on the presence of intact granular glands. The mucous gland component seems to be masked in intact skin, depending partly upon the season and concentration of NE. Ionic dependencies of the mucous gland responses have been studied; they do not seem to involve simple diffusion potentials from Na, K. Cl, or H. The recovery speed from NE stimulation depends on HCO3, being much faster at higher HCO3 concentrations. Supported by NSF GB7668.

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MONOSYNAPTIC EXCITATION OF DORSAL SPINOCEREBELLAR TRACT NEURONES BY LOW THRESHOLD JOINT AFFERENTS. S. Lindström and M. Takata. Dept. of Physiology, Univ. of Göteborg, Göteborg, Sweden.

The dorsal spino-cerebellar tract (DSCT) is known to have subgroups of neurones relaying signals from muscle spindles, Golgi tendon organs and different types of cutaneous mechanoreceptors. Intra- and extracellular recordings from DSCT neurones in Clarke's column in the cat (antidromically activated from the anterior lobe of cerebellum) have now revealed that there is also a group of neurones activated from low threshold joint afferents. The cells were monosynaptically excited from low threshold afferents in the posterior nerve of the knee joint. These afferents take origin in Golgi endings of the joint ligaments and in Ruffini endings of the joint capsulae. Both receptors are slowly adapting and their adapted frequency is a function of the joint angle. It has previously been shown that low threshold joint afferents project to the cerebral cortex of the cat (Körner, L. and S. Landgren, Acta physiol. scand. 1959, 76, 5A-7A). The present findings suggest that information from these receptors is utilized also in cerebellar function.

1030 NEUROGENIC HISTAMINERGIC VASODILATATION IN THE HIND LIMB OF DOGS. F.Lioy,
B.Graham. Dept. of Physiology, University of British Columbia, Vancouver,
B.C., Canada.

After section of the corresponding dorsal roots, electrical stimulation of the intact ventral roots (VR) (L5,6,7) induced in the vascularly isolated homolateral hind limb of dogs, perfused at constant flow, a vasodilatation (VD) (avg. decrease of perfusion pressure (PP): 28.0% of control in 74 trials). A VD of lesser degree (22.7% avg. decrease of PP in 46 trials) was observed also in the controlateral limb. The response was not affected by intra-arterial administration of atropine or propranolol, in doses which abolished the VD induced by acetylcholine or isoproterenol. Intra-arterial Benadryl drastically reduced or abolished the response to VR stimulation and to test doses of histamine. In these experiments acetylcholine and isoproterenol still induced VD. The possible role of histaminergic fibers in the production of the described VD is discussed. (Supported by grant of the B.C. Heart Foundation).

1031 ION CONTENT, K+ FLUX AND CABLE PROPERTIES OF MYOTONIC, HUMAN, EXTERNAL-INTERCOSTAL MUSCLE, R.J. Lipicky and S.H. Bryant, Dept. Pharmacol., Univ. of Cinc., Ohio 45219, U.S.A.

Isolated external intercostal muscle from 11 patient volunteers with clinically evident myotonia and from 13 normal volunteers was studied. Six of the patients showed features consistent with the diagnosis of Myotonia Congenita, and 5 with Myotonia Dystrophica.

Muscle from patients with Myotonia Congenita had cable properties like those of intercostal muscle from goats with hereditary myotonia (J. Gen. Physiol., $\frac{50}{20}$: 89, 1966, J. Physiol., $\frac{204}{20}$: 539, 1969), i.e., mean resting membrane resistance 2 to 3X normal and unchanged mean total fiber capacitance. Compared to normal, the mean K⁺ content was 10% greater, and the mean K⁺ efflux was unchanged.

Muscle from patients with Myotonia Dystrophica had a 6% lower mean water and an 18% lower mean K^+ content than normal muscle. The mean resting membrane resistance was not different from normal but the mean total fiber capacitance was 1.5% normal. The mean K^+ efflux was not different from normal.

These findings suggest that, as in goats with hereditary myotonia, there is a decreased Cl permeability associated with Myotonia Congenita. The findings further suggest that the ultrastructural changes of dystrophy may be associated with a high fiber capacitance. (Supported by NIH grants NS-06782 and NS-03178)

- THE MYOCARDIUM CONTRACTION FUNCTION SELF-ADJUSTMENT. V.A.Lishchuk. Inst.of Cybernetics, Ukrainian Academy of Sciences, Kiev, U.S.S.R.
 - 1. The heart pumping function heuristic model embrases wider scope of physiological and biophysical phenomena, than the algorithm of functioning developed earlier /Lishchuk, 1967/. The model enables one to study the adaptation processes and the phenomena of myocardium progressing deficiency.

 2. The model identifies the heart adaptation system with extreme, selfadjusting automatic control system.

 3. Experimental estimates of the myocardium contraction function in different heart working conditions, moderate and heavy loads, reflex responses, adrenaline influence under different ratios of venous return and arterial counterpressure, are in accord with model testing results.

 4. Heart self-adjustiment system links, central nerve and hormonal systems with intra-cardiac servo-mechanism and biochemical supply of the contraction function.

 5. Heart adaptation mechanism is distinguished in the findings of extreme-value and its structure is similar to self-control system.

 6. Under changing hemodynamics and widely varying nerve-humoral control the self-adjustment process provides the maximum cardiac output for given conditions of heart functioning.

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REDISTRIBUTION OF PULMONARY BLOOD FLOW DURING IMMERSION. M.Litman*, P.Cerretelli, A. Chinet, D.W.Rennie and L.E.Farhi. Dept. of Physiology, State University of New York at Buffalo, USA.

The more even distribution of alveolar ventilation (\dot{V}_A) during head-out immersion as deduced from the reduction in amplitude of the cardiogenic oscillations (c.o.) for argon, indicated that a concomitant redistribution of pulmonary blood flow (Q) is necessary in order to explain the equalization of \dot{V}_A/\dot{Q} throughout the lung. The distribution of Q was studied by observation of the amplitude of the c.o. of oxygen, carbon dioxide and a tracer gas (argon) in the alveolar plateau. Ventilation-induced differences across the lung were eliminated by rebreathing five tidal volumes of a mixture containing 80% argon and 20% oxygen. The subsequent c.o. after 20 seconds of appea apparently reflected the inequality of gas composition produced by the inhomogeneity of Q in the vertical lung. However, the c.o. amplitude, which represents the relative uptake from well and poorly perfused lung regions, was slighter when the subject was submerged than when he was out of the water. The results are consistent with the concept that better perfusion is achieved in apical lung regions during submersion. This supports our thesis inferred from a graphic analysis of the diagram of V_A/\dot{Q} isopleths.

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CHANGES IN THE CAPILLARY FILTRATION COEFFICIENT OF THE RABBIT DURING THE FIRST WEEK OF LIFE. R.A. Little, Experimental Pathology of Trauma Section, MRC Toxicology Unit, MRC Laboratories, Carshalton, England.

It was found when studying the changes in the blood volume of the rabbit with age that the true intravascular plasma volume could not be accurately measured during the first 48 hr of life by the injection of labelled albumin because it rapidly equilibrated with an extravascular albumin space (Little, J.Physiol. 1970, 208, 485-497). This rapid extravasation of injected protein in the new-born rabbit may be a result of a greater capillary permeability and/or capillary surface area at this age. A measure of these two factors is the capillary filtration coefficient (C.F.C) which is the proportionality constant relating the net fluid movement through to the pressure difference across the capillary wall. The C.F.C. was measured in the intact hind limb of 1-day and 5-day-old rabbits using a water filled occlusion plethysmograph. The measurements were performed at the appropriate thermoneutral temperatures. The C.F.C. in the 1-day-old rabbit (0.033 \pm 0.004 ml/min/mm Hg/100 g tissue) was significantly greater (P < 0.01) than in the 5-day-old rabbit (0.013 \pm 0.003 ml/min/mm Hg/100 g tissue). The implications of these results will be discussed.

IMMUNOLOGICAL STUDIES ON THE TRANSPORT, STORAGE AND RELEASE OF THE HORMONE-BINDING PROTEIN NEUROPHYSIN.

B.G. Livett, L.O. Uttenthal and D.B. Hope. Dept. of Pharmacology, University of Oxford, U.K.

Neurophysins are hormone binding proteins of the neurosecretory vesicles which store oxytocin and vasopressin in neurones of the mammalian hypothalamo-neurohypophyseal system (HNS). We have used antibodies against a purified neurophysin to reinvestigate some aspects of neurosecretion. Immunofluorescence histology has been used to localize neurophysin in sections of the HNS of several mammals and microcomplement fixation has been used to investigate some quantitative aspects of neurophysin storage and release. Neurophysin occurred throughout the HNS and its distribution followed the known distribution of neurosecretory material determined by conventional light-microscopical methods. It was present in highest concentration in the axon terminals which surround capillaries in the neurohypophysis. Evidence that it was transported to these terminals by axoplasmic flow from the hypothalamic nuclei was provided by experiments where it was found to accumulate proximal to a constriction of the neurohypophyseal tract. use of an antibody specific to porcine neurophysin-II it has been shown that this neurophysin (1) originates principally from perikarya in the supraoptic nucleus and (2) is released from the neurohypophysis together with lysine vasopressin by a K stimulated, Ca dependent mechanism. The results support the view that neurosecretion from the posterior pituitary involves exocytosis of the contents of the neurosecretory vesicles.

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1036 FUNCTIONAL PROPERTIES OF FROG CEREBELLAR PURKINJE CELLS RECEIVING BILATERAL VESTIBULAR INPUTS. R. Llinás and W. Precht. Div. Neurobiol., Dept. Physiology & Biophysics, Univ. of
Iowa, Iowa City 52240, U.S.A., and Max-Planck-Institut f. Hirnforschung, Neuro-Anatomische
Abt., Frankfurt/M., W. GERMANY.

The electrical activity of Purkinje cells in the frog (Rana catesbeiana) was recorded in the vestibular cerebellum during horizontal constant angular accelerations of different amplitudes. Purkinje cells responding to both ipsi- and contralateral rotation (type III) were found throughout the posterior rim of this cerebellum. These cells were organized such that a topographical relationship exists between the magnitude and directionality of their response and their position in the cortex. Thus, cells in the cerebellar midline showed a response very similar in amplitude and duration for stimuli in the ipsi- or contralateral direction. As the recording electrode was moved laterally to one side or the other, the Purkinje cell activations became asymmetrical and showed a definite bias toward ipsilateral rotation. The type of firing pattern found in these Purkinje cells during rotation ranged from rather phasic to purely tonic. These two types of responses could be encountered in Purkinje cells in immediate proximity of each other. The firing characteristic for a given cell was shown, however, to be the same for ipsi- or contralateral stimulation. This finding implies that the tonic or phasic characteristics of Purkinje cell firing are mainly related to the individual electrophysiological properties of each cell rather than to the physiological properties of the vestibular input.

ON THE EXTRAVASCULAR COMPONENT OF CORONARY VASCULAR RESISTANCE. W.Lochner, W.K.Raff and F.Kosche. Physiologisches Inst., Univ. Düsseldorf, Germany.

There are three main factors, which influence the extravascular component of resistance to coronary inflow: heart rate, intraventricular pressure rise and left ventricular enddiastolic pressure. In experiments with 18 narcotized dogs the three factors were analyzed quantitatively. The intravascular component was stabilized by maximal dilatation. When heart rate was inhanced (auricular pacing) there was an increase of resistance of 14 % for 100 beats/min. (Resistance at 150 beats/min resulted to 0,266 mm Hg x min x 100g x ml and was set 100 %). An increase of dp/dtmax (intracoronary infusion of isoproterenol) of 1000 mm Hg/sec was followed by an increase of resistance of 7 %. (Resistance at 4000 mm Hg/sec resulted to 0,284 mm Hg x min x x 100g x ml and was set 100 %). LVEP was raised by blood transfusion combined with application of a barbiturate. Resistance increased 11 % for 10 mm Hg LVEP rise. (Resistance at 10 mm Hg resulted to 0,269 mm Hg x min x 100g x ml and was set 100 %).

RESPONSE CHARACTERISTICS OF THE CAT'S OTOLITH ORGAN. P. R. Loe and D. L. Tomko. Dept. of Pharmacology, Univ. of Pittsburgh, Sch. of Med., Pittsburgh, Penna., U. S. A.

Anatomical studies have suggested that convergence occurs between macular receptor, cells and first-order afferent fibers. An attempt was made to determine the extent to which such convergence may affect the output of the sacculus and utriculus by recording the activity of first-order vestibular fibers in cats under pentobarbital anesthesia. Stimuli consisted of slow rotations about the naso-occipital axis (roll) and the interaural axis (pitch), as well as sequences of maintained positions. It was found that a population of fibers exists whose responses are consistent with the hypothesis that discharge rate is a function of the shearing force of the otolith on the kinocilium of the receptor cell. The responses of fibers of this population are characterized by regular discharge patterns, and show little adaptation. The response of a given fiber to pitch and roll stimuli can be expressed by a sensitivity vector lying in the plane of its corresponding macula. Fibers originating in the sacculus and in the utriculus can be distinguished from one another on the basis of their responses to roll stimulation. Fibers of this population thus behave as though they receive their input from a single macular receptor cell, rather than convergent inputs. (Supported by AFOSR-66-1005C & MH 11114-04)

MACROMOLECULES INDUCE INCREASED SODIUM TRANSPORT IN RAT CECUM. K.Loeschke, E. Uhlich and R. Halbach. Med.Univ.Poliklinik und Med.Klinik, 5 Köln-Merheim, Ostmerheimerstr. 200, Germany.

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An example of luminal factors controlling the transport characteristics and morphology of the intestinal epithelium may be the increased sodium-coupled water transport and organ enlargement observed in the cecum of germfree rats. To test the hypothesis that these changes are induced by the presence of large molecules, non-absorbable polyethyleneglycol (PEG,mol.wt. 4 ooo) was added to the drinking water of conventionally-raised adult Wistar rats. Compared to controls kept on tap water, a 2-3 fold increase of cecal dry weight and gross surface area was produced by PEG feeding for up to 8 weeks, and a 2-5 fold increase of net sodium-coupled water transport/cm² or mg dry weight, as measured by an in vivo sac technique. Similarly, the transmural potential difference and the steady state concentrations for sodium, chloride and bicarbonate but not for potassium were significantly altered. This is compatible with a concept of enhanced active sodium transport. Aldosterone, sodium-depletion and dehydration do not seem to be involved so that the intermediate steps between luminal macromolecules and the phenomena described are as yet unknown. (Supported by DFG grant Lo 114/5)

TRANSFER OF INSULIN INTO THE BILE IN RABBIT LATE PREGNANCY.C.Lopez-Quijada, P.M.Goñi and L.Chiva. Instituto Gregorio Marañon, C.S.I.C. Madrid, Velaz-quez, 144. Spain.

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Bile insulin of normal and pregnant rabbits has been studied and compared with the plasma insulin levels. The mean hepatic bile insulin of non-pregnant controls was 21 $\mu\text{U/ml}$ and plasma insulin was 25 $\mu\text{U/ml}$. The insulin levels in the hepatic bile increase during pregnancy to 34 uU/ml; in late pregnancy the IRI levels in plasma were about twice as high as non-pregnant levels. The increase in the concentration of insulin in gall bladder bile is of great significance. The passing of insulin from plasma into the bile during late pregnancy follows the same process as in normal conditions, as regards the time required for the insulin to reach maximum values in the bile, but the concentration of insulin in bile was approximately twice as high in the pregnant rabbit than in the control group. The interpretation of biliary insulin values are discussed in the light of an appraisal of the hepatic clearance of insulin.

EFFECT OF ORAL CHLORPROPAMIDE ON THE CIRCADIAN CYCLES OF SERUM IMMUNOREACTIVE INSULIN (IRI) AND GLUCAGON (IRG) AND OF CORTISOL IN MAN. L. Loreti, T. Sugase and P.P. Foà. Dept.of Research, Sinai Hosp. Detroit, Mich. 48235, USA.

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Single doses of sulfonylureas cause insulin release but the results of prolonged treatment may be hyperfunction of the pancreatic islets and increased response to insulinogenic stimuli or, according to some workers, decreased insular activity. We studied the problem in 6 normal subjects under approx. normal living conditions avoiding unphysiologic stimuli such as a glucose load. Blood samples were taken every hour for 72h. and every 15' for 1 h. following 3 nutritionally identical daily meals. Serum 1R1 and 1RG, minimal during the early morning rose after each meal. Cortisol was highest at breakfast time. After 14 d. of chlorpropamide (C) treatment, these patterns were not changed, but the sums of all 1R1 and 1RG values were decreased, that of all cortisol values was increased. The results, suggesting that treatment with C does not enhance insular function and may decrease it, will be discussed in relation to the current controversy on the oral therapy of diabetes. Aided by Chas. Pfizer and the NIAMD.

1042 EFFECTS OF X-IRRADIATION ON THE ELECTRICAL ACTIVITY IN CO-INHIBITED FROG SCIATIC NERVES. J. R. Lott and W. J. Thompson. Dept. of Biological Sciences, North Texas State University, Denton, Texas 76203

The purpose of the work was to shed more light on the nature of the radiation insult to nerve tissues i.e. purely physical vs. metabolic. It has been shown that CO-inhibition of the action pds in isolated nerves can be reversed in light. Such reversal indicates the presence of light-sensitive reactions involved with the electrical properties in nerve membranes. An attempt was made to reverse CO-inhibition of the action potential by exposing the nerves to dosages of x-irradiation known to $\underline{\text{in-crease}}$ the amplitude of the action pds in isolated frog nerves (6 kr/min). We failed to observe such a reversal with x-irradiation, however, it was found that CO did reversibly alter the response of the nerves to x-irradiation and vice-versa. The data clearly indicate that specific metabolic reactions may be involved in the radiation insult and that the radiation effect may not be completely "physical" in nature.

1043 DEPOSITION AND CLEARANCE OF INHALED PARTICLES IN THE HUMAN TRACHEOBRONCHIAL TREE. Ruy V. Lourenço. University of Illinois College of Medicine and the Hektoen Institute for Medical Research, Chicago, Illinois, USA.

Aerosols of particles tagged with gold 198 were produced in a spinning disk atomizer and administered to 85 subjects. Thorax counts and photoscintigrams were obtained with a scintillation camera for 6 hours after inhalation and analyzed with a computer. Deposition of particles in the lungs was found to be dependent on the characteristics of the particles, the pattern of breathing and the value of airway resistance. The pattern of distribution obtained was compared with that derived from mathematical formulas for deposition by impaction and sedimentation. Tracheobronchial clearance was completed in the first 24 hours and presented two successive phases: fast, which lasted approximately 2 hours, and slow, which terminated between 6 and 10 hours following inhalation. The amount cleared in the fast phase increased when particles were deposited mainly in the proximal generations of the tracheobronchial tree. Hyperventilation and cough tended to increase the rate of clearance. Significant abnormalities of the pattern of clearance were found in smokers and patients with chronic bronchitis.

THE EFFECT OF VENTROMEDIAL HYPOTHALAMIC LESIONS ON PLASMA INSULIN LEVELS AND GLUCOSE TOLERANCE OF RATS. A. Løvø and B.E. Hustvedt. Physiol.Branch, Inst. of Nutr.Res., Univ. of Oslo, Norway.

Plasma levels of immunoreactive insulin (IRI), glucose, cholesterol and triglycerides were determined in unrestrained rats equipped with chronically implanted venous catheters. Lesions were then made bilaterally in the ventromedial hypothalamic area by means of electrolysis. Food intake was restricted in order to prevent hyperphagia. An elevated IRI level with no concomitant change in blood glucose was demonstrated two days after lesions in all of the animals used. The plasma triglyceride level increased, whereas the plasma cholesterol concentration did not show consistent changes. Simultaneous hyperinsulinemia and normoglycemia indicate that lesions in the ventromedial hypothalamic area may decrease the ability of insulin to lower the blood glucose level. This possibility was tested by intravenous glucose tolerance tests performed on a series of animals before and after lesions had been made. Glucose tolerance was impaired after lesions in all animals tested. It is concluded that destruction of the ventromedial hypothalamic area in adult rats affects the metabolism even when hyperphagia is prevented by restricted feeding.

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AMMONIA PRODUCTION IN MUSCLE: THE PURINE NUCLEOTIDE CYCLE.

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Experiments will be reported which throw new light on the problem of ammonia production by muscle. Extracts of rat skeletal muscle produce ammonia from aspartate in a cyclical reaction sequence under conditions which mimic muscle doing work. The cycle consists of the reactions catalyzed by adenylate deaminase, adenylosuccinate synthetase, and adenylosuccinase. In harmony with this conclusion is the finding that ammonia production from aspartate shows a catalytic requirement for either IMP, or AMP, or adenylosuccinate. The net effect of the "Purine Nucleotide Cycle" is the formation of fumarate and ammonia from aspartate, and, more indirectly, from glutamate.

The functions of the Purine Nucleotide Cycle fall into several overlapping categories: (1) It is a pathway for the liberation of ammonia from amino acids; (2) it is a pathway for the adjustment of the levels of citric acid cycle intermediates; (3) it is a pathway for regulating the relative levels of AMP, ADP, and ATP; (4) it is a pathway which aids in the control of phosphofructokinase activity, and hence of glycolysis.

INTRACORTICAL DISTRIBUTION OF RENAL BLOOD FLOW IN DOGS BEFORE AND AFTER SALINE EXPANSION. E.W. Løyning. Inst. Exper. Med. Res., Univ. of Oslo, Ullevaal Hosp., Oslo, Norway.

Expansion of extracellular volume by saline infusion is accompanied by an increase in renal blood flow (RBF), glomerular filtration rate (GFR) and sodium excretion (UNa·V). Intracortical redistribution of renal blood flow has been suggested as being responsible for these changes in renal functions (Barton et al. 1968). For further investigation of this problem, before and after intravenous infusion of 30 ml/min 0.9% NaCl blood flow was measured in outer and inner parts of cortex (OCF and ICF) in 5 dogs by polarographic recordings of hydrogen desaturation rates with platinum electrodes placed 2-3 mm and 6-7 mm deep in the renal cortex. Following 45-75 minutes' infusion of saline, urine flow increased from 1.3 ml/min to 8.3 ml/min, on average, and RBF measured with an electromagnetic flowmeter rose from 172 ml/min to 221 ml/min; OCF and ICF increased from 3.28 ml/min·g and 3.48 ml/min·g to 3.76 ml/min·g and 3.90 ml/min·g, respectively. The difference between OCF and ICF was not significant, either in control or after expansion. It is concluded that no significant redistribution of blood flow occurs in the renal cortex during saline expansion, and it cannot therefore be the cause of increased natriures is.

ON THE ROLE OF BICARBONATE IN CATION TRANSPORT IN RED BLOOD CELLS. H. Lubowitz, Washington Univ. Sch. of Med., St. Louis, Mo., U.S.A.

Human red blood cells have been used as a model transport system to examine the relationship between bicarbonate and sodium and potassium transport. Media bicarbonate concentrations were varied over a wide range by substitution of this anion for chloride; pH was kept constant using a gasometric pH-stat apparatus which provided the appropriate CO2 tensions. Both active and passive components of sodium and potassium movement were evaluated as a function of media bicarbonate concentration. ²⁴Na influx and ²⁴Na efflux increased progressively as media HCO3- was raised from 0 to as high as 90 mM/L. ⁴²K influx also increased and the increased rates of cationic transport were accompanied by parallel increases in glycolytic rates. These findings were not due to an increase in pCO2 as the latter was associated with a decrease in unidirectional flux rates. Since the chloride ratio across the cell membrane did not appear to be influenced by the concentration of HCO3 in the media, it seems unlikely that changes in electrical potential could be held responsible. While these changes could be due to the formation of NaHCO3 pairs as suggested by Wieth (Acta Physiol. Scand. 1970, 79: 76-87), the data seem most consistent with a direct effect of HCO3 on the membrane with a resultant alteration in permeability.

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1048 STUDIES ON NEGATIVE POTENTIAL DIFFERENCES (-PD) IN THE TOAD BLADDER. J. H. Ludens and D. D. Fanestil. Dept. of Med., Univ. of Calif. at San Diego, La Jolla, Calif., U.S.A.

Previous studies demonstrated that amiloride (AM) added to the mucosal media of toad bladders (incubated in Ringer's solution containing 24 mM HCO $\bar{3}$ gassed with 5% CO $_2$ - 95% O $_2$, pH = 7) produced -PD that could be inhibited by antimycin A but were not affected by Ouabain. Also, the drug was found to induce -PD even though SO $_4$ replaced Cl $^-$ in the media bathing the mucosal surface of the bladders. In the present studies, the effect of removing serosal K $^+$ and the effect of acetazolamide on AM induced -PD were assessed. AM (10-4 M) induced -PD persisted following removal of K $^+$ from the media bathing the serosal surface of the bladder. In contrast, AM induced -PD of -33 mV (range = -14 to -56 mV) and short-circuit current (scc) of -33 μ A (range = -12 to -59 μ A) in 7 bladders incubated in the 24 mM HCO $\bar{3}$ solution were almost entirely inhibited by addition of acetazolamide (10 $^-$ 3 M) to the serosal media. By 30 min. after acetazolamide addition, -PD were reduced to -2 mV (range = +1 to -5 mV) and scc to -1 μ A (range = 0 to -3 μ A). The -PD dependence on CO $_2$, its independence of mucosal Cl $^-$ and serosal K $^+$, and its inhibition by antimycin A and acetazolamide support the suggestion that the -PD observed after AM are due to an active secretion of H $^+$ and provide the first evidence to suggest that the epithelial cells of the toad's bladder, like the distal renal tubule, are capable of secretion of H $^+$.

1049 EVIDENCE FOR CENTRAL TIMING OF RHYTHMICAL MASTICATION. J. P. Lund and P. G. Dellow. Dept. of Physiology, University of Western Ontario, London, Canada.

The origin of the rhythm and co-ordination of mastication, traditionally ascribed to alternating activity in two peripheral reflex arcs, was investigated in the rabbit. Bursts of activity were recorded from the mandibular and hypoglossal nucleus in phase with masticatory movements caused by electrical stimulation of the corticobulbar pathways. These bursts occurred alternately in nerves to jaw opening and jaw closing muscles. Regularly recurring bursts of evoked activity within the hypoglossal nucleus were unaffected by paralysis, severing branchial nerves, cranial nerves and the spinal cord and the use of stimulus pulse trains of random frequency. The frequency of occurrence of bursts was independent of the average stimulation frequency over a wide input range. Mechanical deformation of the brain of vascular or respiratory origin was discounted as a source of the rhythm. It was concluded that rhythmical masticatory movements are co-ordinated by a brain stem pattern generator which is not dependent on peripheral feedback for the timing of this cyclical motor activity.

TRANSMISSION OF THE TRANSMYOCARDIAL PRESSURE AS A FUNCTION OF THE OS-CILLATION FREQUENCY. P.P.Lunkenheimer, H.Keller, W.Rafflenbeul, H.H.Dickhut Physiologisches Institut der FU, Berlin 33, Arnimallee 22, Deutschland.

In order to calculate the external work of the heart, it is necessary to know the transmural ventricular pressure. This is a difficult problem because of the difficulties in measuring the pericardial reference pressure and the problem caused by the non-linear, transmyocardial transmission of the oscillation of the extracardial pressure to the intracardial pressure. An oscillation of the pressure was created in the thoracic cavity by inducing a sinusoidal excursion of the thorax with a frequency range of 2-32 cps, and the transmission characteristics of the myocardium was examined by comparing the amplitudes of the peri- and intracardial pressures. An intracardial increase in amplitude, dependent on the frequency, could be determined during the continuously changing functional state of the myocardium during the heart action. The maximum amplitude of the intracardial pressure occurred in the relaxation phase when the frequency of the extracardial oscillations was 17 cps. The first maximum in the ejection phase occurred at 26 cps. At 31 cps the amplitude was increased during the entire period of contraction, with a peak occurring in the isometric phase.

BINDING OF PHYTATE TO HEMOGLOBIN. <u>J.Luque</u>, <u>M.E.Ventura</u> and <u>A.Santos-Ruiz</u>. Department of Biochemistry. Faculty of Pharmacy. Madrid University. Spain.

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The concentration of phytate in avian erythrocytes is similar to that of 2,3-diphosphoglycerate (2,3-DPG) in humans. In the presence of phosphate there is a decrease in the affinity of the hemoglobin for oxygen. Experiments on this line have shown that both phosphocompounds are bound to the respective oxyhemoglobin; chicken oxy-Hb binds phytate in a higher ratio than human oxy-Hb, being the binding affected by the ionic strength of the solvent used; sheep or goat oxy-Hb have a lower molar binding ratio according to the absence of these phosphates in their red cells. It seems to us that phytate could play a similar role to that of 2,3-DPG as physiological system for the regulation of the oxygen affinity. Binding experiments were carried out by the equilibrium dialysis technique at physiological conditions.

RESPONSE OF GASTRIC VESSELS ON ARTERIAL AND VENOUS PRESSURE ELEVATION (AUTOREGULATION AND VENO-VASOMOTORIC REACTION)

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The fact that the stomach is supplied by different vascular ways may cause, that in this area autoregulation could not yet be demonstrated. No informations are available concerning reactions on venous pressure elevation. Perfusing the coeliac artery in the cat (with all nongastric vessels - specially those of spleen, duodenum and liver ligated) it was possible to obtain true reversible increases of resistance with arterial pressure elevations. Pressure-flow curves with the typical concavity to the pressure axis could also be received. The phenomenon was seen in 19 out of 30 tests in 6 cats (autoregulation in 63.3%). In the positive reactions a rise of flow of 69.6% was accompanied by an arterial pressure increase of 80.4%. An increment of resistance generally appeared only above a perfusion pressure of 70 mm Hg. — Venous pressure elevations of 22 mm Hg showed constrictions in 58 out of 64 tests in 10 cats, that means veno-vasomotoric reactions in 90.6%. In the mean of these perfusions with flow held constant an arterial pressure increase of 44.8 mm Hg occurred, in some cases more than 75 mm Hg. Like in other vascular beds the venous triggered reactions were more violent; this fact is to be seen as a protection mechanism against further large inflow in case of venous congestion.

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IN VITRO RAT GUT TRANSMEMBRANE POTENTIALS. I. Lyon and H. E. Sheerin, Sci. Div., Bennington Col., Bennington, Vt., U.S.A.

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These studies were carried out to develop a routine procedure for microelectrode recording of transmembrane (transmucosal and transserosal) potentials (PD's) across the intestinal epithelial cell of small mammals. With the microelectrode (tip potential, < ± 5 mV; tip resistance, $30-70M\Omega$; tip diameter, about 0.3μ) and ancillary instrumentation, in vitro cell impalements of rat gut preparations give stable, reproducible transmembrane PD's which respond rapidly to changes in the composition of the bathing media. For example, the jejunal transmucosal PD (mean ± S.E.) is -9.44±0.12mV (n=790 impalements) in the absence of glucose and -9.73±0.70 mV (n=46) in its presence (20mM; corrected for osmotic disequilibrium against 20 mM D-mannitol). The corresponding transserosal PD's are -12.42±0.12mV (n=790) and -17.34±0.67mV (n=46). Quantitatively similar data have been obtained with ileal preparations. The minus signs indicate intracellular negativity with respect to mucosal or serosal reference =0. Thus, the transmural PD values, calculated as the algebraic difference between transmembrane (transmucosal-transserosal) FD's are +2.98mV and +7.61mV, respectively. The sugar-induced increment of transmural potential, +4.63mV, is similar to such values measured directly. Glucose, as other actively transported sugars, enhances the transserosal PD, with little or no effect upon the transmucosal PD. Preliminary studies of the transmembrane effects of ouabain show a much greater influence upon the transserosal PD than upon the transmucosal PD. These findings are consistent with the concept of an electrogenic ion extrusion mechanism acting at the serosal border of the intestinal epithelial cell.

AIRWAY RESISTANCE IN ASTHMA ON EXERCISE. H.A.LYONS, and S.Steen. Pulmonary Disease Division, Department of Medicine, State University of New York, Brooklyn, N.Y., U.S.A.

Ten asymptomatic asthmatic subjects were studied at rest and on exercise Determinations of alveolar-arterial gradients for oxygen tension (A-aD $_{\rm O2}$), dead space-tidal volume ratio (VD/VT), alveolar ventilation (VA), oxygen consumption (VO $_{\rm 2}$) and carbon dioxide production (VCO $_{\rm 2}$) were made. Airway resistance (R $_{\rm A}$) measured by whole body plethysmography was elevated (mean 3.5 cmH $_{\rm 2}$ O/L/sec).

After the resting determinations were made the patients exercised on a treadmill at 3 1/2 m.p.h. on a 20% grade for 3 1/2 minutes. Repeated determinations were made and $R_{\rm A}$ was observed to have decreased 30 to 50% of control resting value (mean 1.5 cmH₂O/L/sec). The other determinations also changed consistant with the improvement of $R_{\rm A}$.

The results of this study, differs from previous reports, in that we observed decrease of airway resistance on exercise instead of an increase. The decrease in airway resistance is accompanied by improved alveolar ventilation.

1055 QUANTITATIVE STUDY ON THE INTRACELLULAR PATHWAYS OF PROTEIN ABSORPTION BY THE KIDNEY. T. Maack. Dept. of Physiol. Cornell Univ. Med. Col., N.Y., N.Y. USA

Administered lysozyme (LY-MW,14,000) is absorbed by proximal tubular cells of the mouse kidney.Differential centrifugation experiments show that absorbed LY is distributed in two intracellular compartments:in large phagosomes(P) and in the cytoplasmic sap(S).At high i.p. doses of 0.5-1.0 mg LY/gm BW (average concentration in kidney cortex:46.7 µg LY/mg protein) the average LY content in P was 51%±4.4(tSE) while that of S was 46%±3.3 of the total LY tissue content.At low doses of 0.05-0.20 mg LY/gm BW(8.8 µg LY/mg protein in kidney), the fractional contents of LY changed (p<0.01) to 22%±2.5 in P and 64%±3.6 in S.Thus, there was an inverse relationship between dose and fractional content of LY in S. In addition, transfer of lysosomal enzymes to the sub-cellular fraction containing LY in P (formation of phagolysosomes) could only be demonstrated at the high doses of LY. Since only the fraction of LY remaining in phago-lysosomes will be subjected to the action of hydrolytic enzymes, present results support the hypothesis (Maack and Kinter, Am.J.Physiol,1969) that transcellular transport of intact protein is the major way by which the kidney handles normal protein loads while catabolism of absorbed protein would occur in conditions of protein overload.

1056 INTERACTION BETWEEN GUSTATORY PAPILIAE OF THE BULLFROG TONGUE. John A. Macdonald. Dept. of Zoology, Univ. of California, Los Angeles, Calif. 90024, U.S.A.

Bullfrog (Rana catesbeiana) glossopharyngeal nerve fibers each innervate 4-6 fungiform papillae; each papilla receives 2-4 separate fibers. Interaction between papillae has been demonstrated by other workers, and may serve as a model for peripheral integrative mechanisms. Electrical stimulation of a single papilla reveals three excitability phases following each suprathreshold stimulus in a given fiber: (1) a refractory period of 2-4 msec; (2) a facilatory period (110% normal excitability) from 5 to 20 msec after stimulus; (3) a depressed period from 20 to 3-400 msec after stimulus, with minimum excitability (ca. 75%) around 50 msec. Antidromic impulses originating in a connected papilla or in the glossopharyngeal nerve cause similar excitability changes, but do not appreciably affect invasion of the nerve terminal. No such pattern is seen when the 1st stimulus is subthreshold; increasing the 1st stimulus to 3X threshold produces the same changes as near-threshold stimuli. Separate fibers in a given papilla have independant thresholds and excitability cycles. Thus one receptor can either facilitate or depress activity of a connected receptor; the mechanism of interaction is apparently in the receptor/nerve junction.

FRICTIONAL INTERACTIONS IN RED CELL MEMBRANES. Robert I. Macey and Robert E.L. Farmer.
Department of Physiology, University of California, Berkeley, California 94720, U.S.A.

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The Kedem-Katchalsky equations (J. Gen. Physiol. 45:143, 1961) relating the experimental membrane parameters (L_p , σ and ω) to frictional coefficients have been exploited in an effort to assess the relative intensities of solute, solvent and membrane interactions during passive transport. In principle the hydraulic water permeability L_p should depend on \overline{C}_s , a weighted mean concentration of penetrating solute. To date experiments with beef red cells show that this dependence is very weak. The result can be interpreted by assuming that the frictional interaction between solute and membrane is much less than the interaction between solute and water. This implies that the reflection coefficient is independent of the dynamic frictional parameters and depends only on the equilibrium properties of the membrane. The results can be interpreted in terms of small water filled channels which restrict the lateral motion of solute. (Supported by NSF GB 11981 and Bay Area Heart Research Committee.)

INTRACELLUIAR K + ACTIVITY AND ELECTROGENIC PUMP OF A BARNACLE PHOTORECEPTOR. H. Mack Brown and A.M. Brown, Depts. of Physiol. and Cardiol., Univ. of Utah, College of Nedicine, Salt Lake City, Utah, U.S.A.

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Analyses of the membrane potential changes that occur during and following illumination in B. eburneus indicate that the depolarizing receptor potential is associated with a membrane permeability increase mainly to Na ions (J. Physiol. 208: 385-413), whereas the post-illumination-hyperpolarization (PIH) is due to an electrogenic Na pump initiated by an increase of internal Na concentration during illumination (Fed. Proc. 29: 393). An alternative mechanism for PIH was suggested by the current-voltage relation of the membrane during PIH, i.e., the outward membrane current associated with PIH was reduced at positive membrane potentials. Thus PIH could be due to a conductance decrease to one ion species such that the membrane potential approaches a large negative value determined by the distribution across the membrane of another ion species. Since the distribution of K ion could explain the large negative e.m.f., the internal and external K ion activities were measured with liquid ion-exchanger microelectrodes. Internal K activity for eight cells was 90.25 mM, (S.E. 3.02 mM) which yields a mean calculated E_{ν} of -68.5 mV (S.E. 0.87 mV). This value was much less than the maximum membrane potential during PIH (in some cases up to -100 mV). This result provides additional evidence for the conclusion that PIH is produced by an electrogenic Na pump and the current-voltage relation of the membrane during PIH may be an expression of the voltage dependance of this pump.

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ELECTROPHYSIOLOGICAL ASSESSMENT OF ODOR INTENSITY. P. Mac Leod et A. Pesez Lab. de Physiologie des Sensibilités Chimiques et Régulations Alimentaires Collège de France, Paris, France.

A new method of simultaneous intensity matching in the unanesthetized

A new method of simultaneous intensity matching in the unanesthetized rabbit has been developed, which takes advantage of reciprocal inhibition between olfactory bulbs. It consists of presenting the two stimuli in exact synchrony on both nostrils and simultaneously recording the two evoked bulbar potentials. When the intensities on both sides are exactly matched, the two evoked potentials have the same amplitude. Owing to reciprocal inhibition, this situation is critical and even a slight difference (about 10 %) in concentration results in a conspicuous squeezing of the potential on the less stimulated side. This method has been used for measuring different kinds of quantitative interactions in binary odor mixtures.

1060 CLIMBING FIBER RESPONSES EVOKED IN THE FLOCCULUS BY VISUAL PATHWAY STIMULATION IN THE RABBIT. K. Maekawa & J. I. Simpson. Dept. of Physiology, Fac. of Med., Univ. of Tokyo, Tokyo, Japan.

Visual influences upon the vestibulo-cerebellum were studied in the anesthetized rabbit (pentobarbital, 35 mg/kg). With glass microelectrodes inserted into the flocculus, typical climbing fiber (CF) field and unit potentials were recorded following electrical stimulation of the optic chiasm (latency, 11-12 msec). Similar CF responses were recorded following stimulation of the contralateral brachium of the superior colliculus (latency, 10-11 msec). Flash illumination also evoked CF responses. Bilateral ablation of the visual cortex had no detectable effect upon the visual evoked CF responses, but the chiasm response was abolished by sectioning the contralateral brachium of the superior colliculus. Contralateral inferior olive (IO) stimulation also evoked CF responses in the flocculus. Facilitation and occlusion between the CF responses evoked from the IO and from the visual pathway showed that the visual evoked CF responses in the flocculus were mediated by the contralateral IO. After the brief facilitation period, visual pathway stimulation produced a marked, long-lasting (about 100 msec) inhibition of the IO evoked CF response. The findings demonstrate that visual information, passing through the midbrain, enters the flocculus as climbing fiber activity via the contralateral inferior olive.

1061 DIFFERENCE IN THE EFFECTS OF ATROPINE AND SCOPOLAMINE ON NEUROMUS-CULAR TRANSMISSION. T. Maeno and S. Hashimura. Dept. of Physiology, Faculty of Med., Kagoshima Univ., Kagoshima, Japan.

Certain difference in the effects on neuromuscular transmission has been noted between atropine and its closely related drug, scopolamine. Atropine not only diminished and shortened the end-plate potential (EPP) but also shifted the equilibrium potential for EPP towards positive membrane potential. On the other hand, scopolamine depressed and prolonged the EPP without alteration in the equilibrium potential for EPP. To study the ionic mechanism of the above drug effects on the EPP, the end-plate currents (EPCs) were recorded on the glycerol treated frog muscles with voltage-clamp technique. The EPC-membrane potential relation was linear over the wide range of the membrane potential. This fact strongly suggested that the end-plate conductance change during neuromuscular transmission might not be dependent on the membrane potential. The EPCs obtained at the equilibrium potential for K ions, the time course of which should be identical with that of Na conductance change during the end-plate activity, were simply shortened with atropine while distinct initial fast and later small sustained phases appeared with scopolamine. The EPCs recorded at the equilibrium potential for Na ions, whose wave form should reflect that of K conductance change during neuromuscular transmission, were affected rather inversely with the two drugs. The EPCs consisted of two phases in atropine and lacked the slow phase in scopolamine.

1062 HOW THE RETINAL CHANNELS BUILD UP THE GENICULATE RECEPTIVE FIELDS.

L. Maffei and A. Fiorentini. Laboratorio di Neurofisiologia del C.N.R.,
Pisa-Italy.

From previous studies, the following properties of the antagonistic surround of the retinal ganglion cell receptive field are known: (1) it disappears after dark adaptation; (2) in response to sinusoidal modulated light it shows a cut-off at a temporal frequency which is much lower (15 cps) than that of the center of the receptive field (about 40 cps). Our experiments at geniculate level show: (1) the antagonistic surround of geniculate cells does not disappear after dark adaptation; (2) it shows a cut-off at a temporal frequency which is as high as that of the center of the receptive field (around 35-40 cps). The conclusion drawn from these experiments is that both the centers and the antagonistic surrounds of geniculate cells reflect the properties only of the centers of the retinal ganglion cell receptive fields. It seems unlikely therefore that the main role of the organization of retinal receptive fields is the enhancement of contrast.

INHIBITION OF SODIUM TRANSPORT BY PROPIONATE. R.H.Maffly, A.Taylor and J.J.Hess. Depts. of Med., Stanford Univ. and V.A. Hosp., Palo Alto, Calif., USA.

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In contrast to the reports of other workers, we have found that under appropriate conditions propionate inhibits rather than stimulates active sodium transport by the toad bladder. Evidence has been obtained from transport and metabolic studies for two theories of action. (1) Propionate may divert energy away from the sodium pump through a mechanism involving its conversion to, and subsequent oxidation of, succinate: It is well established that oxidation of succinate in mitochondria is associated with reversal of electron transport through site I in the electron transport chain (Chance and Hollunger, JBC 236:1534, 1961). We postulate that in the toad bladder ATP formed at site I is preferentially utilized by the sodium transport mechanism; oxidation of propionate via succinate, by reducing the rate of ATP produced at site I, reduces energy available for sodium transport. (2) Propionate may decrease the mucosal permeability to sodium: Since propionate inhibits sodium transport when added to the mucosal surface, it appears to be decreasing the rate of passive entry of sodium across this surface of the cell, thereby reducing the rate of delivery of sodium to the presumed serosal pump site. This property is shared by other fatty acids and appears to be due to interaction between the fatty acids and some component of the mucosal membrane. The interrelationship of these two possible mechanisms is currently being explored.

DIFFERENT SENSITIVITY TO HEPARIN ANTIHEMOSTATIC ACTION.J.R.Magalhaes, Carmem V.S.Unglert and I.Roisenberg(São Paulo).Dept.of Physiology and Pathology, Fac.Ciências Médicas Sta Casa, SP, Brazil.

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Besides its anticoagulant activity heparin has an antihemostatic action indicated by a bleeding time greater than 30 minutes after intravenous injection of 200-300 IU/kg. Humans and animals (dogs and rabbits) present a wide variation in sensitivity to this heparin action. Only 19 percent of the dogs, 12 percent of the rabbits and less than 5 percent of humans are heparin-sensitive. In over 200 tests it was demonstrated that the degree of sensitivity could be easily detected by a topical test with heparin solution. Preliminary analysis in over eighty families are suggestive that this trait is inherited in humans. Heparin antihemostatic action is probably due to an inhibitory action on myosin ATP-ase activity in the bleeding local, since ATP was able to block heparin antihemostatic action when topically applied in humans.

ACTION OF TSH ON THE SERUM PBI AND TYROSINE LEVEL. V. Magazinović, M. Hamam=+ džić, S. Adilović, F. Pandža. Inst. of Physiology, Veterinary Faculty, University of Sarajevo, Sarajevo, Yugoslavia.

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Serum tyrosine concentration is increased in patients and experimental animals with hyperthyroidism and decreased in subjects suffering from hypothyroidism. The mechanism underlying these changes is not entirely clear, but there are indications that TSH, as a factor regulating the distribution of tyrosine between serum and thyroid tissue, could play the important role Under influence of TSH the synthesis of thyroid hormone could be enhanced through the more efficient supply of thyroid gland with tyrosine. The thyproxine produced might in turn alter further synthesis by reducing intra

glandular free tyrosine as well as suppressing TSH release.

The results of our experiments support this hypothesis. We have investigated simultaneously the serum tyrosine level and the serum PBI before and after application of TSH. During the period up to 9 hours following the TSH application, the concentration of serum PBI increases and in the same time the concentration of the serum tyrosine decreases. After this period, the significant decrease in serum PBI concentration is runing parallel with the increase in the serum tyrosine level. 12 hours after the application

of TSH, serum tyrosine concentration become higher than Before.

1066 THE SECRETION OF PEPSIN. D.F. Magee. Creighton University School of Medicine, Omaha, Nebraska, U.S.A.

It has been variously held that gastrin and gastrin pentapeptide do or do not stimulate pepsin secretion from denervated gastric corpus pouches. In dogs with gastric fistulae and denervated pouches, if the wash-out technique of collection from the pouch is used, pentagastrin, tetragastrin and caerulein are without effect on pouch pepsin secretion. Feeding or the introduction of acetylcholine into the pyloric antrum or intravenous 2 deoxy d glucose will increase pouch acid secretion but will not stimulate pepsin. Pouch pepsin secretion is stimulated by secretin or by the administration of ganglionic blocking agents or muscarinic ganglionic stimulants with pentagastrin. We have concluded that to stimulate pepsin, gastrin and its derivatives require cholinergic activity of a muscarinic ganglionic type.

1067 CHOLINERGIC MECHANISM RESPONSIBLE FOR ACTIVATION OF VESTIBULAR NEURONES AND RAPID EYE MOVEMENTS IN DECEREBRATE CAT. P.C. Magherini, O. Pompeiano and U. Thoden. Istituto di Fisiologia, Cattedra II, Università di Pisa, Italy.

The main aim of this study was to investigate the neuropharmacological mechanism responsible for activation of second order vestibular neurones leading to rapid eye movements. In precollicular decerebrate cats single vestibular neurones discharged quite regularly. Intravenous injection of physostigmine sulphate (0.1 mg/Kg) greatly modified the pattern of discharge of some vestibular units, which showed groups of rhythmic bursts of rapid firing alternated with periods of inhibition. These groups of rhythmic bursts (1) were separated by intervals in which the unit discharged regulary, (2) were related in time with trains of rapid eye movements, and (3) occurred at a regular rate of about one every two sec and continued up to 15-25 min. In the same preparation there was also a tonic suppression of the decerebrate rigidity. The units affected were located in the medial and descending vestibular nuclei. However units localized in the lateral vestibular nucleus of Deiters did not show any change in the pattern of discharge in spite of the occurrence of bursts of eye movements. These findings indicate that a cholinergic mechanism, probably reticular in origin, is responsible for excitation or disinhibition of the vestibular units. The inhibitory connections existing in the neural networks within and between the vestibular nuclei probably represent the basic inherent mechanism responsible for the periodic rhythmic changes in the vestibular discharge.

THE RELATIVE SIGNIFICANCE OF PRE - AND POSTSYNAPTIC EFFECTS IN MONOSYNAPTIC EXTENSOR REFLEXES FOLLOWING VIBRATION OF A SYNERGIC MUSCLE. P.C. Magherini, O. Pompeiano and U. Thoden. Istituto di Fisiologia, Cattedra II, Università di Pisa, Italy.

This study illustrates a condition in which presynaptic inhibition is associated with postsynaptic facilitation. In decerebrate cats, high-frequency longitudinal vibration of the soleus (S) muscle produced reflex contraction of the vibrated muscle, as well as DRP in the lumbar cord, due to depolarization of the group Ia extensor afferents (PAD). Vibration of the S muscle for 150-200 msec (at 300/sec, 70-100 μ amplitude) was used as a conditioning stimulus on heteronymous monosynaptic test reflexes (MRs) of comparable amplitude. The induced facilitation, maximal for the medial gastrocnemius MR, progressively decreased for the plantaris, flexor digitorum longus and tibialis reflexes. The medial gastrocnemius and plantaris MRs were facilitated throughout the vibration and were followed by a prolonged inhibition. On the contrary the flexor digitorum longus and tibialis MRs were facilitated only during the early part of the vibration and were often followed by a delayed inhibition, which outlasted the duration of the stimulus. This inhibition had the same time course of the induced PAD. It is concluded that the reduced postsynaptic efficacy of the orthodromic Ia volleys due to PAD overwhelms the postsynaptic excitation of the extensor motoneurones only in those instances in which the degree of heteronymous monosynaptic interconnection is small.

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THE ACTION OF Ca⁺⁺ UPON THE MECHANISM OF ACTION POTENTIAL GENERATION IN THE SOMA OF MOLLUSC NEURONES. <u>I.S.Magura</u>, <u>O.A.Krishtal</u>. Institute of Physiology, Ukrainian Academy of Sciences, Kiev, USSR.

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An increase in the external $[{\rm Ca}^{++}]$ often causes a decrease in the overshoot of the action potential and increase the rate of its fall. Voltage clamp experiments prove this effect to be due to earlier and considerable increase in the potassium conductance of the membrane. Preceding depolarization eliminates this effect. Preceding hyperpolarization affects voltage-dependent potassium conductance in the same way as the high $[{\rm Ca}^{++}]$. It is possible to suggest that in some cases $[{\rm Ca}^{++}]$ can take part in the transfer of the inward current. Considerable increase in $[{\rm Ca}^{++}]$ in the sodium-free solution sometimes restores the action potential generation. The high values of the transient inward current are observed in such cases under voltage clamp condition. This phenomenon may be due to some reconstruction that takes place in the membrane under the influence of the high $[{\rm Ca}^{++}]$.

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FATIGUE AND RECOVERY IN ISOLATED SKELETAL MUSCLES. G.W. Mainwood and Pauline Worsley-Brown, Dept. of Physiology, University of Ottawa, Ottawa, Canada.

Twitch tension and contraction velocity in isolated skeletal muscles decrease as much as 90% following repetitive stimulation. The early studies of Fletcher and Hopkins showed that, after fatigue, tension recovers in the presence of oxygen. Experiments were carried out to identify the rate limiting steps in the oxidative recovery process. Isolated, superfused, frog sartorius muscles were frozen and analysed at intervals after stimulation to fatigue and during recovery. At the same time potassium and lactate fluxes were measured. Recovery is accelerated by high (25 meq/1) bicarbonate concentration and lactate efflux is increased about threefold while potassium efflux is reduced. A secondary decline in tension to reach a minimum after about 15 min. is consistently seen in low bicarbonate solutions. This corresponds with the end of the rapid phase of creatine phosphate synthesis. ATP levels do not appear to be an important limiting factor. Calculations based on proton source and sink reactions indicate that intra cellular hydrogen ion balance is the main factor limiting recovery of twitch tension. (Supported by Medical Research Council of Canada).

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SPINAL INFLUENCES ON BARORECEPTOR REFLEXES. AJIT MAITI. Dr. B.C.Roy P. G. Inst.of Basic Med.Sciences. Calcutta University, Calcutta-20, INDIA.

In low spinal vagotomized cats occlusion of bilateral common carotid artery provoked a reproducible pressor response associated with increased stroke volume which did not parallel changes in respiration. This response was demonstrable when the basal blood pressure in spinal cat was above 80 mm Hg.It was augmented following strychnine treatment but was abolished after complete deafferentation of carotid sinus region. The depressor response produced by carotid sinus stretch was potentiated in spinal cat and was reduced following bilateral vagotomy. The pressor response evoked by sciatic stimulation or bladder distension in spinal cats was markedly enhanced during carotid occlusion. Also, the peripheral sympathetic discharges from splanchnic nerve elicited during carotid occlusion in spinal animals was increased by sciatic stimulation. These data demonstrate the existence of some spinal influences which would effectively participate in the modulation of baroreceptor reflexes depending on the relative balance of supraspinal drive and the excitatory state of the spinal vasomotor centers. It is concluded that apart from classical sinus nerve, the sympathetic innervation of carotid sinus might have some afferent route for signalling the baroreceptor discharges to spinal cord.

DISCRETOMETRY AND ADEQUATOMETRY IN THE MEASURING OF RESOLVING CAPACITY IN SENSE ORGANS OF MEN. P.O. MAKAROV. CHAIR OF BIOPHYSICS OF THE LENINGRAD UNIVERSITY. LENINGRAD, USSR.

We designated the discretness - the intermittence of sensations as the minimal critical interval between two adequate and inadequate stimulations of the sense organs.

The period between two sensations during which it is impossible to distinguish their succession was called by us in 1935 as "the interval of the present". Its duration depends on the analyser stimulated, the character of the stimulus and the functional state of the organism. Our knowledge about the external environment depends on the resolving capacity of the sense organs. The temporal parameter of resolving capacity is determined by a critical discrete interval which varies from 30 to 100 msec. The critical discrete interval may serve as a test of a man functional state. Its increase is the historial result of discase, fatigue, negative emotions etc.

1073 ATP SYNTHESIS BY THE SARCOPLASMIC CALCIUM PUMP. Madoka Makinose Abt. Physiologie, Max-Planck-Inst.für med. Forschung, Heidelberg, Germany.

In EGTA containing media, the sarcoplasmic vesicles preloaded with calcium release the calcium extremely slowly. Addition of ADP and Pi activates the release of calcium strongly and, simultaneously, ATP is synthesized from ADP and Pi. For ATP synthesis, calcium preloading is essential besides the presence of ADP and Pi. The close relationship between ATP synthesis and calcium release suggests that these reactions are the reversal of the ATP dependent sarcoplasmic calcium accumulation. As expected, increasing of the ATP or the calcium concentration in the assay prevents calcium release and ATP synthesis. Magnesium, an essential activator for the active calcium accumulation, is also indispensable for calcium release depending ATP formation. Prenylamine, an inhibitor for the calcium uptake, inhibits the rate of calcium release and ATP synthesis to the same extent. The temperature coefficient is the same for the forward and reverse calcium translocation and coupled phosphate turnover between 10° to 25°C (Q_{10} = \sim 5). Synthesis of one molecule ATP is strictly correlated with the downhill translocation of two calcium ions. The participation of mitochondrial contaminations is excluded.

1074 EFFECT OF ISOPROTERENOL AND CYCLIC AMP ON RNA SYNTHESIS IN MOUSE PAROTID AND KIDNEY. Daniel Malamud and Jean Paddock. Surg. Serv. Mass. Genl. Hosp. and Dept. Surg. Harvard Med. School. Boston, Mass. U.S.A.

A single injection of isoproterenol (IPR) stimulates DNA synthesis in mouse parotid and kidney. In both tissues the growth response is preceded first (1-4 hours) by a decreased and later (8-12 hours) by an increased incorporation of 3H-uridine into RNA. In parotid, there is evidence that the early apparant decrease in RNA synthesis is due to an alteration in the UTP pool. Within minutes after injection of IPR there is an increase in adenyl cyclase activity and a resultant elevation of cyclic 3',5' adenosinemonophosphate (cAMP) levels. Injection of dibutyryl cyclic AMP results in a depression in RNA specific activity in both parotid and kidney within 1 hour. When the drugs are administered in vivo, and 3H-uridine incorporation measured in an in vitro slice system, there is no decrease in 3H-uridine incorporation. Studies with RNA polymerase isolated from mouse kidney demonstrated no change in enzyme activity after IPR or cAMP either in vivo or in vitro. These results are consistent with the hypothesis that the decreased incorporation of 3H-uridine after injection of IPR is a cAMP-mediated pool effect. Supported by grant p-534 from the American Cancer Soc. and the Shriners Burns Institute.

BLOOD pH, P_{CO2} AND BICARBONATES IN HIBERNATING HAMSTERS. <u>A. Malan and H. Arens</u>. Lab. Physiologie Respiratoire, C.N.R.S., Strasbourg, France.

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Indwelling carotid catheters were placed in 12 European hamsters, Cricetus cricetus. Between mid-September and mid-November, arterial pH and P_{CO_2} were measured (and $[HCO_3^-]$ calculated) on 20 blood samples taken from euthermic, gently restrained animals (colonic temperature 37.0 - 38.6 °C); the mean values \pm 2 S.E. were: pH = 7.40 \pm 0.01; P_{CO_2} = 45.3 \pm 3.0 torr; $[HCO_3^-]$ = 28.3 \pm 1.8 mM·L⁻¹. Between mid-October and mid-December, 10 arterial blood samples were obtained during hibernation from 4 out of the 12 animals, whose cheek-pouch temperature was 8.5 - 10.0 °C; values for pH were 7.57 \pm 0.01; for P_{CO_2} , 36.1 \pm 6.1 torr; for $[HCO_3^-]$, 53.8 \pm 8.6 mM·L⁻¹. Blood pH and $[HCO_3^-]$ were significantly raised, and P_{CO_2} significantly decreased in hibernation as compared to euthermia. This is in contrast with the review by Reeves and tends to approach the values reported for ectotherms.

LEARNING PROCESSES IN PRAYING MANTIS. H. Maldonado and J.C. Barrós-Pita. Inst. Venezolano de Investigaciones Científicas, Caracas, Venezuela.

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The possibility that some items of behaviour in the praying mantis could be modified by experience was analyzed. Three patterns of behaviour were studied: 1) the turning of the head when the insect was faced with an indifferent stimulus; 2) the attack of the mantis on a moving object; 3) the deimatic reaction, i.e. a frightening response that is displayed when a mantid is faced with a foe. To study 1) and 2), a special device was used to record automatically head movements and number of attacks. To study 3), mantis were faced with the back projection of filmed shiny cow-birds silhouettes. A learning process with a long retention was found as regards items 2) and 3), but the turning of the head seems to be an incoercible response that only accepts short lasting modifications. Results are discussed in connection with the role that different parts of the compound eye plays in the behaviours under study.

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SPECTROPHOTOMETRY OF THE CHOROID IN THE ALBINO RABBIT. P. Malessa, J. Peregrin, and J. Svěrák. W.G. Kerckhoff-Herzforschungsinstitut der Max-Planck-Gesellschaft, Bad Nauheim, Bundesrepublik Deutschland.

Fundus spectrophotometry was performed in the inact albino rabbit eye, the refractive power of the cornea being eliminated. Areas of 4 mm2 were selected, and illuminated by a highly monochromatic light. The wavelength of the light changed continuously between 450 and 700 nm. The reflected light was measured. The extinction spectra obtained from the fundus areas exhibited all spectral characteristics of hemoglobin, In vitro experiments showed that the thickness of a layer of undiluted or diluted blood can be calculated from the spectrophotometric data using the Lambert-Beer equation and the extinction coefficient of a standard hemoglobin solution for green-blue light (505 nm). From in vivo experiments introducing stepwise dilution of the circulating blood it is concluded that the Lambert-Beer equation is valid for calculating the thickness of the choroidal blood layer, too. If the thickness of the blood layer exceeds 250 u as in the choroid of man and if blue, green or yellow light is used, no longer absorption but reflection within the blood is measured. In the albino rabbit the choroidal blood layer is less than 50 u thick (average value: 36 ulin areas near the horizontal meridian. In the lower quadrants maximal values (130 u) were found. Pulssynchronized variations of the blood layer were detectable nearly everywhere in the fundus.

1078 CATECHOLAMINE ENHANCEMENT OF CORONARY BLOOD FLOW FOLLOWING MAXIMUM REACTIVE HYPEREMIA.

G.S. Malindzak, Jr., H.D. Green, G.J. Van Komen and G.B. Orr. Bowman Gray Sch. Med., Winston-Salem, North Carolina, 27103, U.S.A.

Hypothesis: Maximum coronary vasodilation is thought to result in response to reactive hyperemia after a period of maximum myocardial ischemia (MMI). 13 mongrel dogs were tested by measuring coronary blood flow (CBF) and mean aortic pressure (MAP) following maximum i.v. doses of nitroglycerin(NG), isoproterenol(ISO), norepinephrine(NOR) and epinephrine (EPI) given separately and in combination with the response obtained following MMI. The results are summarized in the table below (Qmax=maximum CBF; R=MAP(mmHg)/CBF(ml/min)):

	Drug Alone		MMI Alone		Drug + MMI	
Drug	Qmax ml/min	R at Q _{max} PRU	Q _{max}	R at Q _{max} PRU	Q _{max} ml/min	R at Q _{max} PRU
NG	47	2.68	101	1.17	84	1.29
(% control)	248±42	39 ± 5	667±14	14 ± 1	599±72	17 ± 2
ISO	58	2.2	101	1/17	113	1.15
(% control)	333±60	32 ± 5	677±24	14 ± 1	731±65	14 ± 1
NOR	42	4.39	101	1.17	159	1.03
(% control)	245±23	61 ± 7	677±24	14 ± 1	915±111	15 ± 1
EPI	63	2.9	101	1.17	158	1.04
(% control)	353±18	39 ± 3	677±24	14 ± 1	966±107	15 ± 1

Supported in part by grants from USPHS (HE-487, -5392) and North Carolina Heart Assn.

AFFERENT ACTIVITY FROM THE HEART IN THE SYMPATHETIC NERVES.

A. Malliani, G. Recordati, P.J. Schwartz and M. Pagani. Cardiovascular Res. Inst.,

Univ. of Milan and Cardiovascular Res. Ctr., CNR, Milan, Italy.

Functional properties of cardiac receptors signalling through afferent fibres in sympathetic nerves are almost unknown. In anaesthetised and artificially ventilated cats electrical activity was recorded from single afferent fibres dissected from the third left thoracic sympathetic ramus communicans. Circulatory stimuli consisted in: stenosis or occlusion of inferior vena cava, pulmonary artery or veins, left coronary artery, thoracic aorta; blood volume changes. Only 10% of all recorded fibres had a spontaneous discharge characterized by: a) a constant cardiac rhythm (with no more than one nervous impulse per cardiac beat) and b) a clear relation with atrial or ventricular dynamics. The responses to the various haemodynamic stimuli made often possible to relate the activity of these nervous fibres to one particular heart chamber. The discharge of most of the fibres was also increased during coronary occlusion. Therefore cardiac sympathetic receptors seem to be able to provide nervous centres with highly specific information. However, their pattern of discharge is different from that of cardiac vagal receptors.

MICROPERFUSION STUDY OF TITRATABLE ACIDITY FORMATION IN PROXIMAL AND DISTAL TUBULES OF RAT KIDNEY. G. Malnic, M. Mello Aires, G.B.de Mello and G. Giebisch. Depts. of Physiology, São Paulo Univ., São Paulo, Brazil, and Yale Univ., New Haven, Conn., USA.

Proximal and distal tubules of control rats and of rats submitted to acute metabolic alkalosis (5% NalCO3) or acctazolamide infusion were perfused with 95 mM/l Na2NPO4 completed to isotonicity with raffinose. The fluid columns were isolated with oil, and pl changes were recorded continuously by an antimony microelectrode. pl was proportional to PD between this electrode and a reference glass microelectrode. The increase in NaN2PO4 concentration was calculated on the basis of tubular pl and a pK of 6.8. This concentration approached equilibrium according to one exponential. Its mean half-time was 7.4 sec in control proximal tubule, 7.2 sec in early and 8.5 sec in late distal tubule. In spite of considerably lower distal than proximal rates of sodium reabsorption, I ion secretion is not much different in these tubular segments. In acute alkalosis, steady-state pH values are considerably more alkaline than in controls, but secretion half-times are not significantly different both in proximal and distal tubules. Acetazolamide infusion reduced proximal acidification rate to 53% of controls, early distal rates to 25% and late distal rates to 46%, showing that carbonic anhydrase has an important role also in distal acidification. In all cases there remains a residual acidification rate of considerable magnitude.

RENAL SALT AND WATER EXCRETION IN THE ONE-HUMPED CAMEL G.M.O. Maloiy, East African Veterinary Research Organization, Muguga, Kenya.

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Previous studies on the water balance of the camel have shown that its ability to resist severe dehydration is partly due to the ability of the kidney to excrete a highly concentrated urine (2800m0sm). Quantitative information about renal function in the camel is however lacking. A study was therefore undertaken to examine renal salt and water excretion, and glomerular filtration rate in the camel under a variety of carefully controlled experimental and physiological conditions. Dehydration caused a 57% decrease in urine flow and a 30% reduction in GFR (Cinulin). Salt loading (2.75% NaCl) increased both GFR as well as urine flow by about 52% and 103% respectively (p<0.01). These results are summarized below.

	Urine flow ml/min	Osmolality mOsm/kg H ₂ O	G.F.R. ml/min	N.
Normal hydration	0.56 ± 0.07	1463 ± 121.9	179 ± 9.1	16
Salt loading	1.14 ± 0.02	2049 ± 38.2	272 ± 11.4	16
Dehydration	0.24 ± 0.02	2230 ± 50.8	124 ± 5.2	16

Urine osmolality and osmolal U/P ratio both increased during dehydration. The overall water expenditure during and when the animals were hydrated and dehydrated was examined.

DISTRIBUTION OF PULMONARY BLOOD FLOW DURING CONTROLLED PERFUSION OF THE INTACT LUNG.

J.E. Maloney, T.M. Adamson, B.C. Ritchie, A. Walker. Dept. of Physiology, University of Melbourne, Melbourne, Victoria, Australia.

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The distribution of pulmonary blood flow (Xe 133) and the relation of pulmonary artery pressure to left atrial pressure was studied in the anaesthetised sheep using a double heart bypass preparation. When total pulmonary blood flow was altered but left atrial pressure kept constant, two patterns of distribution of blood flow were observed. In four animals despite large changes in overall blood flow the pattern of distribution of flow remained unaltered suggesting that a constant proportion of the total blood flow perfused the gas exchanging vessels of the lung at each level. In two other animals as blood flow diminished the proportion of total blood flow perfusing the alveoli at each level diminished. In six animals intravascular pressure was increased by raising left atrial pressure during constant pulmonary blood flow. Alveolar perfusion increased throughout the lung, the change being greatest over the uppermost portion. In a further six experiments, alveolar blood flow increased with increasing lung gas volume although pulmonary blood flow was constant. Although pulmonary vascular resistance was constant when left atrial pressure exceeded alveolar pressure throughout the lung, significant hysterisis was evident at lower atrial pressures. This study supports the concept of recruitment of pulmonary capillaries secondary to increases in left atrial pressure and lung volume. Under certain conditions the proportion of flow passing to the alveolus remains constant despite large changes in overall blood flow.

SODIUM-DEPENDENT CHANGES IN THE RENAL ENZYME-PATTERN OF THE RAT.

M. Mályusz, G. Mályusz and B. Ochwadt. Max-Planck-Institute for Experimental Medicine, Department of Physiology, Göttingen, German.Fed.Rep.

1083

Rats maintained on a high sodium diet showed increased activities of enzymes of the tricarboxylic acid cycle (ICDH, MDH) in the renal cortex and to a lesser extent in the medulla. Enzymatic activity of the glycolytic pathway (HK, FDP-ALD, LDH) was highly elevated in the medulla, whereas in the cortex only the aldolase-activity was found to be increased. G-6-PDH showed no decrease either in the cortex or in the medulla. Low dietary sodium did not interfere with the enzymatic activity of the oxydative processes. Rate-limiting enzymes of the glycolytic pathway showed somewhat elevated activities in the cortex, but in the medulla their level remained normal. G-6-PDH-activity was high both in the cortex and in the medulla. Positive sodium balance seemed to raise the renal metabolism generally, whereas low dietary sodium activated mainly the pentose-monophosphate-shunt.....

VENOPRESSOR AND VENODEPRESSOR POINTS IN THE MEDULLA OBLONGATA.

S.K. Manchanda, Physiology Dept., All India Inst.Med.Sci.New Delhi, INDIA

Venous tone changes were recorded in dog's hind limb by the 'arrested circulation' technique with a simultaneous registration of the femoral arterial pressure. Medulla oblongata was stimulated with square wave pulses (2-4 volts, 0.1 msec., 40-80/sec.) by stereotaxic technique so as to permit an exact mapping of the pressor and depressor points. The results indicate a rather diffuse localization of these points. The venopressor and venodepressor points do not conform to the classical "vasopressor" and "vasodepressor" areas in their localization. Instead various combinations of venous and arterial pressure changes were elicited. Ample records were obtained in which stimulation of a medullary point produced a rise in venous pressure accompanied by a fall in arterial pressure and vice-versa. According to the current concept of bulbar control of vascular tone, all the segments of vasculature are lumped together and it is considered by extrapolation that the vasoconstrictor centre stimulation of which produces a rise in arterial pressure will also have a venoconstrictor effect and the vasodilator centre in a similar way will dilate the veins. In the light of these observations, such a concept will need a revision.

1085 INTRACELLULAR STUDY OF INTRALAMINAR THALAMIC NEURONS DURING STIMULATION OF THE BRAIN-STEM. M. Mancia, G. Broggi and M. Margnelli. Inst. of Physiology, Univ. of Milan, and Space Biol. Lab. of CNR. Milan, Italy.

It has been recently shown in intracellular study that stimulation of the brain-stem has a differential input to intralaminar thalamic (Mth) neurons (Mancia et al Brain Res. 25, 638-641, 1971). In this investigation we have further analysed the synaptic properties of Mth neurons during rostral and caudal brain-stem activation, using a Wheatston bridge technique for intracellular stimulation through a glass micropipette filled with 2.2 M K-citrate.

Encéphale isolé cats were used curarized and artificially ventilated.

High frequency stimulation (50-150 c/sec) of mesencephalic reticular structures induced inhibition of firing of an high percentage of studied cells. No membrane conductance changes were seen indicating that disfacilitation may be responsible for such an effect. High frequency stimulation of bulbo-pontine structures could evoke inhibition of firing of some Mth neurons with increasing membrane potential. Intracellular applied current pulse during such an effect has revealed conductance changes indicating a presence of a postsynaptic inhibition.

1086 ELECTRICAL FLUXES IN FROG SKIN UNDER STEADY-STATE VOLTAGE CLAMPING. Lazaro J. Mandel and Peter F. Curran. Department of Physiology, Yale University, New Haven, Conn. U.S.A.

Bidirectional fluxes of Na were measured in skins of rana pipiens, voltage-clamped at intervals in the range -150 to +100mV (hyperpolarized to depolarized). The invout unidirectional flux displays passive diffusion characteristics, but the out+in flux is characterized by three components. Two of these components appear to be related to the active Na transport pathway, while the third one has characteristics suggesting a parallel shunt pathway. If this latter component is subtracted from the total influx, the effect of potential on the Na unidirectional flux through the pump is obtained. The Na flux through the pump has two components: one displays passive diffusion characteristics in response to changes in applied potential, and to changes in external Na and Ca+ concentration: the other component is unaffected by the applied potential, displaying saturation characteristics. The implications of this voltage clamping technique will be discussed in terms of its usefulness in the determination of a Na pump model as well as the site of action of various ions and drugs.

THE RESPONSES OF CELLS IN THE SUPERIOR COLLICULUS TO STIMULATION WITH LIGHT PATTERNS MOVING AT DIFFERENT VELOCITIES. G. Mandl. Aviation Med. Res. Unit, McGill Univ., Montreal, Canada.

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Different parts of a collicular cell's receptive field may have different velocity response characteristics, as well as different stimulus orientation preferences. Extracellular records from units in the stratum griseum superficiale and the stratum opticum of the right superior colliculus in paralyzed cerveau isolé cats were made with metal micro-electrodes. The contralateral retina was stimulated with dark-light borders moving at uniform velocities of 2-400 deg/sec, and amplitudes of 2-20 deg arc. Borders were projected on a screen placed some 40 cm in front of the animal's eye, subtending some 50 deg arc. Unit responses were determined by averaging action potential trains in the form of post-stimulus histograms. Stimulation of a given cell's receptive field "center" resulted in peak responses for pattern velocities between 5-20 deg/sec, and 75-250 deg/sec, with sharp drops in responses between 25-50 deg/sec. Stimulation of the same cell's "surround" only yielded peak responses between 25-50 deg/sec, with responses decreasing toward both ends of the frequency spectrum. Cells responded optimally to a moving border stimulus having a given angular orientation. For a given cell a different orientation preference was found when stimulating (a) the center; (b) the surround; or (c) the combined center-and-surround, of its receptive field. It was not possible to deduce the combined center-surround orientation preference from a knowledge of the separate center and surround response characteristics.

PHASE-RELATIONSHIPS OF CIRCADIAN RHYTHMS: THE CORRELATION OF BODY-TEMPE-RATURE AND REACTION-TIME. H. Mann and J. Rutenfranz, Dept. Int. Med. II, Techn. Univ. Aachen, Dept. Occup. Med. Univ. Giessen, German Fed. Rep.

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The circadian periodicity of oral body-temperature and multiple-choice-reaction-time (Bettendorff apparatus) was investigated in 7 test-persons during 5 periods of one week. Simultaneous measurements of both variables were taken every 4 hours. Both variables exhibited clear 24-hour-rhythms. Shape and phase of the diurnal curves of speed of reaction and body-temperature corresponded to each other. There was a significant negative correlation of all pairs of data of both variables (p<0,001). The calculation of the same data as averages of each day, as well as all data at the same time of day (e.g. all measurements at 1200 o'clock on all experimental days), showed no correlation of both variables. It is concluded that the highly significant negative correlation does not originate in any causal relationship of both variables but in the phase-relationship of their circadian rhythms. These results are of general importance: When measuring biological variables at different times of day it has to be taken in consideration that the employed method of calculating correlations has to be free from any influences of circadian periodicities.

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ON THE WEIGHT OF BOXES CARRIED IN BALI. A.Manuaba and M.Nala. Dept.of Physiology, Faculty of Medicine, Univ.of Udayana, Denpasar, Bali, Indonesia.

In Bali there is no standardization nor strict legislation yet on the weight of loads generally, and on the weight of boxes especially, that may and could be carried by workers. Considering this, relevant to the type of carrier used, a study on the most effective and productive weight of boxes carried has been made. The result indicated that for a 12 meter distance and a replacement of 180 and 300 kg of loads, boxes of 15 kg weight are considered as the most suitable ones (180 kg is the permissable load for a "dokar"-coach pulled by a horse, and 300 kg for a "bemo"-3-wheeled car, and for "pedati"carriage, pulled and pushed by man).

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1091 EFFECTS OF AMYLTRIMETHYLAMMONIUM ON NEUROMUSCULAR JUNCTIONS OF FROG MUSCLE. L. Marco. Dept. Neurol., Col. Physicians&Surgeons, New York, NY, USA.

The various effects of amyltrimethylammonium (ATA) on the electrical properties of single skeletal muscle fibers were investigated in the sciatic nerve-sartorius muscle preparation of the frog by means of intracellular micropipettes. ATA was applied by microperfussion or added to the Ringer's bath. The magnitude of fiber depolarization by microperfussion of junctional zones (70 cells) was related to the concentration of the drug. At all five concentrations (0.02, 0.05, 0.1, 0.2, and 0.5 mM) the amplitude of the miniature end-plate potentials and their rates after perfussion were decreased respect of the control values. These effects were most marked at the higher concentrations (0.2) at which both amplitude and rate were reduced to about 50 per cent of control. Perfussion of 0.5 mM ATA caused violent twitchings and loss of resting membrane potential (RMP). Perfussion of non-junctional sites failed to cause any changes in RMP at all concentrations studied. 0.5 mM bath-applied ATA caused depolarization to -52 mV and the rate of repolarization was fastest, the fibers returning to resting level (-90 mV) within 40 min. Initial depolarization was lowest (to -77 mV) and the rate of repolarization was slowest (100 min) for the lowest concentration (0.02 mM). These findings demonstrate that ATA has a depolarizing power almost as great as that of carbamylcholine, and can be used more conveniently to investigate the problems of activation and inactivation of the post-junctional chemosensitive zone of single muscle fibers.

EFFECT OF CEREBELLAR AGENESIS ON MUSCLE SPINDLE AFFERENT RESPONSES IN CAT.

L.A. Marco, D. Sommers, H.C. Ebel, and S. Gilman. Dept. of Neurology, Col. of Physicians & Surgeons, Columbia Univ., New York, N.Y., USA.

Complete ablation of the cerebellum in the adult cat depresses the responses of muscle spindle primary afferents to stretch of the muscle containing the spindles. The natural occurrence of congenital cerebellar agenesis in cats, now thought to result from maternal infection with feline panleucopenia virus during gestation, provides an opportunity to determine whether a similar disorder of spindle response occurs in the adult cat with cerebellar agenesis. Accordingly, unitary responses of medial gastrocnemius (MG) muscle spindle primary afferents to passive extension of the MG muscle were recorded from dorsal root filaments with the animals lightly anesthetized with pentobarbital. Afferent frequency response/muscle length curves of animals with cerebellar agenesis were compared with those of control, acutely (1 week) decerebellate and chronically (2-3 months) decerebellate cats. It was found that the responses of the cerebellar-agenesis animals were less than those of controls, greater than those of acutely decerebellate cats, and similar to those of chronically decerebellate cats. It is concluded that the feline nervous system compensates poorly for the deficit induced by cerebellar agenesis, despite the fact that the agenesis occurs in prenatal life.

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ALACTIC O DEBT PAYMENT FOLLOWING SUPRAMAXIMAL EXERCISE. R. Margaria, P.E. di Prampero and H Evers. Institute of Human Physiology, University of Milano, Milano, Italy.

It is well known that the oxygen consumption at the end of the exercise decreases very rapidly, following an approximately exponential path, which has the significanece of the payment of the oxygen debt. The area delimited by this curve and the coordinates is indicative of the oxygen debt (alactic) which has been found to amount to about 20 ml/kg of body weight in maximal aerobic exercise. No data however have ever been collected during recovery from a supramaximal exercise. In exercise leading to exhaustion in 5 to 30 secs the recovery oxygen consumption curve has been measured with a rapid oxygen analyzer (mass spectrograph): in this condition the oxygen consumption does not decrease immediately, but it maintains the exercise value for 15 20 secs and the oxygen debt has been found to amount to about 40 ml of D per kg of body weight, a value about twice as high as that measured after aerobic exercise. This amount of oxygen corresponds to 25 mMoles of split phosphagen (ATP+CP) per kg of muscle, which corresponds to about all the phosphagen contained in the active muscles.

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CONTROL OF PUNISHED BEHAVIOR BY ENDOGENOUS ACETYLCHOLINE IN THE HYPOTHALAMUS. D.L. Margules Dept. of Psychology, Temple University, Phila., Pa., USA.

Increase of endogenous acetylcholine in the medial hypothalamus of albino rats, by direct bilateral application of 5-14 µg of the cholinesterase inhibitor, physostigmine hydrochloride (PH), reduces operant responses for food in the punished and the nonpunished components of a multiple schedule of reinforcement. These effects may be due to a specific punishment enhancing action of the drug. Alternatively, they may be the result of a general depressant action. The latter alternative was ruled out by repeating the PH treatment after extinction of the punished behavior. Under this condition, PH had no suppressant effect on operant behavior. When punishment was reinstated, PH suppressed operant behavior once again. Punishment must be present in order for PH to suppress operant behavior. This suggests that punishment causes the release of endogenous acetylcholine in the medial hypothalamus. Treatment with PH may enhance punishment by increasing the accumulation of endogenous acetylcholine in the medial hypothalamus. Enhancement of punishment induced by PH was reversed by direct bilateral application of 5-10 µg of the muscarinic receptor blocker, atropine methyl nitrate, to the medial hypothalamus. Endogenous acetylcholine may enhance punishment by occupation of muscarinic synaptic receptors in the medial hypothalamus.

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SUPPRESSION OF SYNAPTIC TRANSMISSION IN REINNERVATED MUSCLE. R.F. Mark and Lauren R. Marotte, Dept. of Physiology, Monash University, Clayton, Victoria, AUSTRALIA.

After denervation neuromuscular synapses are reformed in multipley innervated skeletal muscle of some lower vertebrates when either the original or a foreign nerve grows back into the muscle. The two kinds of synapse are not morphologically different by electronmicroscopy and separately either one will cause muscle contraction. When both innervations are present in one muscle only the correct nerves work and the incorrect innervation is suppressed. We find no evidence of degeneration of suppressed synapses and no evidence of altered reflex behaviour of foreign motoneurones. Transmission from these synapses is regulated by competitive intercellular recognition processes that operate at a molecular level at the neuromuscular junction. We suggest that the efficacy of many synapses in the central nervous system may be controlled by similar developmental mechanisms even into adult life and that if the recognition process was use-dependent this could form the biological basis of memory.

1096 BIOPHYSICAL ASPECT OF THE PROCESS OF HEMOCOAGULATION AND HEMOSTASIS.

A.A.Markossian. Inst.of Age Physiology, Acad.of Pedagogical Scien., Moscow, USSR.

There is found a straight dependence between the value of z-potential and the tendency of blood to coagulation. This dependence correlates with the concentration of heparin. It may be suggested that the elevation of negative charge of thrombocytes is one of mechanisms of anticoagulant action of heparin. Electrokinetic processes of blood fluctuate under the influence of active substances: hormones, mediators and biologically active amins. Adrenaline serotonin as well as procoagulants decrease the z-potential and acetylcholin, histamine and anticoagulants increase it. During hemostatic and clot formation processes aggregation of thrombocytes takes place when the z-potential is being reduced. The decrease of the last can be to a large extent explained by the appearance of ADF, under the influence of which the negative charge of thrombocytes falls. There are some definite correlative reactions found between the changes of transmural potential of the vessel wall, it's intima and electrokinetic processes of blood. Clear changes of electrokinetic processes, biophysical properties of the vessel wall are found in experimental atherosclerosis and during hypercoagulation. The effect of hypothalamus and autonomic nervous system and biophysical processes, taking place in blood and vessel wall are studied.

WARM AND COLD SENSATIONS AND CHANGES IN SKIN TEMPERATURE PRODUCED BY TRANSIENT THERMAL STIMULI. L. E. MARKS. John B. Pierce Fndn. Lab., New Haven, Conn., U.S.A.

To help clarify the nature of the proximal stimulus for warmth and cold, skin temperature was measured and psychophysical judgments of sensation magnitude (S) were obtained for several intensities (positive and negative) and durations of radiant stimulation of the ventral body surface. At the end of any given constant stimulus duration, S is a power function of the induced change in skin temperature (ΔT) according to the formula $S = k|\Delta T|\beta$. The exponent β depends only slightly on duration, but is consistently larger for cold than for warmth; k, on the other hand, depends strongly on duration. Given any constant intensity, cold increases steadily with duration, but warmth varies relatively little. Of two stimuli that produce identical ΔT , a high intensity-short duration stimulus arouses greater sensation than does a low intensity-long duration stimulus. That is, diminishing sensitivity under continuing radiation can partially offset the ever-increasing stimulation of the receptor systems. The results suggest that time-dependent gain-control mechanisms modulate the sensitivity to temperature changes.

1098 GASTROINTESTINAL MIGRATING ELECTRICAL COMPLEX. J.A.Marlett and C.F.Code. Mayo Clinic and Mayo Foundation, Rochester, Minn., U.S.A.

Szurszewski and Code (Gastroenterology 54:1304, 1968) described a caudally migrating electrical complex of the small bowel of dogs fasted 18 hours. In this study we have observed the electrical activity of the stomach and entire small bowel of dogs during longer fasts and interrupted the electrical complex with various stimuli. Experiments were begun 10 days after implanting AgAgCl electrodes on the serosal surface of the stomach and small bowel and were continued for many months. In all of the 107 complexes studied in 5 animals, the antrum displayed an electrical complex similar to that of the small bowel. Recordings during four 6-hour periods of the 24- to 48-hour segment of a fast showed that in all animals the migrating electrical complex recurred cyclically throughout the 24 to 48 hours. Duration of the cycles ranged from 60 to 150 minutes; 90 to 140 minutes were required for the complexes to migrate from the stomach to the terminal ileum. Interruption of an electrical complex by inflation (400 ml) of a rubber balloon in the stomach stopped caudad migration of that complex and initiation of other complexes in only 1 of 4 dogs tested. However, the interdigestive electrical pattern was always disrupted for 1 to 1½ hours by a 400-ml water instillate and for 2 to 3½ hours by a 400-ml milk instillate. (Supported in part by NIH Grant AM-2015.)

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CHANGES IN ASCORBIC ACID AND CALCIUM METABOLISM IN MEDULLOADRENALECTOMI-ZED GUINEA-PIGS. C.Marnay-Gulat, M. Dam Trung Tuong et Y. Raoul. Lab.de Physiologie, Fac.de Pharmacie, Paris, FRANCE.

Five weeks after medulloadrenalectomy guinea pigs excrete about 50 p.cent less noradrenaline and adrenaline than normal animals. They need more vitamin C in the diet : 20 mg/day are necessary to prevent hemorrhages and to restore normal growth. Despite this supplement, blood ascorbic acid and adrenocortical stores in vitamin C are lower than those of control animals receiving the same basal diet and the same ascorbic acid supplement. Blood calcium is lowered to 7 mg p.cent and the injection of 200 USP of parathyroid hormone has no effect on the calcemia of the medulloadrenalectomized guinea pigs; this dose is active on control animals. Urinary and fecal calcium excretions are not significantly different in normal or medulloadrenalectomized guinea pigs.

MICROPUNCTURE STUDY OF FLUID & ELECTROLYTE TRANSPORT IN THE MALE REPRODUCT-IVE TRACT.D.J.Marsh & N.Levine.N.Y.Univ.Med.Ctr., New York City, U.S.A.

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Micropuncture technics were used to study single seminiferous tubules (ST) the epididymis (e), and vas deferens(VD) of the rat. ST contain a fluid that is slightly hypertonic, has higher K and Cl, lower Na, and is slightly acid relative to plasma. ST lumen is 5 mV negative to interstitium, so K & Cl enter against electrochemical gradients, while Na entry is downhill(which does not preclude active transport of Na). Between ST and beginning of E, spermatocrit changes indicate that 50% of the fluid leaving the ST is reabsorbed. Cl & K concentrations in reabsorbate are higher than lumen concs., Na in reabsorbate is the same as in lumen, and H+ is secreted. This region has same electrical potential as ST, so that Na and Cl reabsorption are contragradient, but K reabsorption is downhill; organic acids are secreted. E and VD reabsorb 50% of remaining fluid.Na conc. in reabsorbate is higher than lumen conc., K enters the lumen, and pH rises. Na and Cl reabsorption occur at different sites, and so are not coupled. E is 20 mV negative to interstitium, VD is 27 mV negative. Reabsorption if Na is contragradient as is K entry, and there appears to be secretion of organic compounds.

Supported by NIH Grant AM 06864

METABOLIC ACIDOSIS AND MYOCARDIAL CONTRACTILITY. J. C. Marsiglia, H. E. Cingolani, N. González and E. Marincevic. Inst. of Physiology, La Plata, Argentina.

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In order to elucidate controversies about the effect of metabolic acidosis upon myocardial contractility experiments have been designed with this metab olic change in the Starling Heart Lung preparation (HLP). The myocardial contractility was characterized by means of the variations in the left ventri-cular and diastolic pressure(LVEDP), a segment of the left ventricular circumference(LVCS) and the development of the maximum velocity of the left ven tricular pressure(dP/dt) while the stroke work was kept constant. After a control period, Ringer solution(100 cc/1 blood) titrated pH 1 through the ad dition of HCl, were added to a series of preparations and the same solution but without HCl(pH 7.4) to another series of them. The study of the regression between the relation pH-LVEDP was:

(P<.01) (r=-.6)

LVEDP=133-(17.1±5).pH
The relation pH-aH was:

LVEDP=2.5+(.12±.034).aH⁺ (P<.01) (r=.6)
When Ringer solution pH 7.4 was added the parameters used as an index of contractility remained constant during all the experiments. Metabolic acidosis produces a negative inotropic effect upon NLP within the range studied (pH 7.4-7.0). Although it is a small change, the variations are statistically significant.

1102 THE MOTIVE ACTIVITY OF THE DIGESTIVE TUBE IN THE FOSTER-CHILD (électrosplanchnography method). A.MARTIN et J.L.THILLIER, Laboratoire de Neurophysiologie et pathologie psychosomatique, C.H.U Bretonneau, 37-TOURS. (France) (en relation avec le Laboratoire de Physiologie : Pr. J. THOUVENOT et Service de Pédiatrie : Pr. COMBE).

The motive activity of the digestive tube can be derived at the surface of the skin of the abdomen by mean of metallic electrodes adequately disposed.

The variations of potential so obtained at the nursling are of vity which the origin had may be specified by correlation effected with the observed pictures grace to the radiocinematograph: 3 per minute for the stomach, 3 to 4,5 for the antropylaric, 6 to 10 per minute for the small intestine, I all the five minutes at 3 per minute for the colon.

By elserwhere the pharmacodynamic agents which depress the mechanical activity of the intestine made equally disappear the electrosplanchnography activity. The rythme activitys order of special manner at the time of physiological events which may be anticipated : gastro-colic reflex but above all vesico colic reflex.

At last, these studies effected at the nursling, demonstrate that this last, at the buth, present a digestive tube which the motricity introduced by an rythme activity E.S.G identical at those of normal adult.

INFLUENCE OF THYMECTOMY ON RENAL ELECTROLYTE EXCRETION PATTERNS OF MALE 1103

HOODED RATS. Constance R. Martin. Dept. Biol. Sciences, Hunter Col., CUNY, Park Avenue, New York, N.Y., U.S.A.

Male hooded rats of our colony maintained on powdered Purina laboratory chow and 1% Sodium Chloride ad libitum in individual metabolism cages in a temperature controlled room, exhibit short and long range cycles in renal excretion of sodium, potassium, chloride and water. Significant variations in absolute amounts excreted as well as in percentages of intake excreted and in urinary Na:K ratios have been found in all rats tested. Inorganic phosphate excretion does not parallel patterns for monovalent ions. The phosphate excretion does not parallel patterns for monovalent ions. The cycles persist in the presence of bilateral adrenalectomy or unilateral nephrectomy, and seem to be independent of environmental lighting. Removal of the thymus gland exaggerates the variations, especially in adrenalectomized animals. Urinary electrolyte values are lower for thymectomized—adrenalectomized than for sham thymectomized—adrenalectomized rats when values for the latter are low; thymectomized—adrenalectomized rats tend to excrete larger quantities of electrolytes than do sham thymectomized—adrenalectomized rats when values for the latter are high. Although melatonin is believed to affect electrolyte excretion through some influence on adrenabelieved to affect electrolyte excretion through some influence on adrenocortical secretion, preliminary data indicate that thymectomy markedly affects the urinary electrolyte response of adrenalectomized rats to the injection of melatonin.

THE EFFECT OF MONOVALENT CATIONS ON THE SODIUM SENSITIVE CHOLINE FLUX IN HUMAN 1104 ERYTHROCYTES. K. Martin. Dept. Pharmacology, University of Cambridge, Cambridge, England.

The influx of choline into human erythrocytes is reduced and the intracellular concentration of choline no longer rises above the extracellular concentration when the sodium in the incubation medium is replaced by lithium or potassium; conventional analysis of the results suggests that removal of external sodium reduces the apparent affinity of the transport system for external choline. However, the composition of the external medium will also affect the unidirectional efflux of choline from the cells: replacing up to 30 m-equiv/l of sodium by lithium reduces the efflux while substituting the sodium by potassium has little effect. Replacing between 30 and 150 m-equiv/1 of sodium by either lithium or potassium leads to a progressive increase in the efflux of choline. This effect of external cations on choline efflux is most pronounced when the external medium is free of choline; it is no longer observed when the external concentration of choline is 0.2 mM or higher. A small fraction of the internal cations can be replaced by lithium by leaving cells overnight in a lithium buffer. The unidirectional influx of choline into these cells is reduced and the kinetics of the influx suggest that the presence of lithium in the intracellular phase reduces the apparent affinity of the transport system for external choline but has little effect on the maximum rate of transport. The results cannot be explained by the hypothesis that the sodium gradient determines the net flux of choline simply because the affinity of the carrier for choline at either side of the membrane is controlled by the concentration of sodium on that particular side.

LANTHANUM IONS ON THE GIANT SYNAPSE OF THE SQUID. R. Martin & R. Miledi. Stazione Zoologica, Naples, It., & Dept.of Biophysics, Univ.Col.London,UK.

1105

The synapse between 2nd and 3rd order giant axons in the stellate ganglion of the squid is a chemical synapse which operates by release of an as yet unidentified transmitter. When La³+ions (1-5 mM) are added to the seawater bathing isolated ganglia, presynaptic nerve impulses continue to invade the terminals but fail to release transmitter, presumably because La³+interferes with the inward movement of calcium which is necessary for transmitter release by membrane depolarization. Spontaneous miniature synaptic potentials can still be recorded, thus showing that the postsynaptic membrane remains sensitive to the transmitter. La³+also causes a large and rapid rise in frequency of miniature synaptic potentials followed by a marked decrease suggesting that transmitter quanta are being exhausted. Electron-microscopic study of synapses treated with La³+revealed a progressive decrease in the number of synaptic vesicles. In most respects the effect of La³+on squid synapses resembles that at neuromuscular junctions (Heuser & Miledi). Since different transmitters are involved at these synapses it seems that La³+acts generally at chemical synapses by blocking transmitter release by nerve impulses, and causing an increase in frequency of miniature potentials leading to exhaustion of synaptic vesicles in the terminals.

THE RELATIONSHIP OF PLASMA URATE CONCENTRATION TO OVIDUCT FUNCTION IN THE DOMESTIC FOWL (GALLUS DOMESTICUS). L.Martindale and W.G.Siller. Agricultural Res. Council's Poultry Res. Ctr. West Mains Road, Edinburgh EH9 3JS, Scotland.

1106

The wide range of plasma urate levels in the domestic fowl can be explained only partly by changes in reproductive condition, dietary nitrogen level and food consumption; much variation remains unresolved. Measurements of the plasma urate levels of normal laying hens and of similar birds put out of lay by injections of F.S.H. confirmed that reproductive activity in the hen lowers the mean plasma urate concentration. Detailed studies of the plasma urate levels in fasted laying hens in relation to the time of oviposition showed a marked depression in plasma urate during the build-up of protein in the magnum of the oviduct. This suggests that the proteins of egg albumen are synthesized from the same metabolic pools of nitrogen as the plasma urate. It further suggests that plasma urate levels depend more on metabolic activity in the oviduct and on dietary factors than on renal activity.

DEVELOPMENT OF THE RELATIONSHIP BETWEEN GLOMERULAR AND TUBULAR FUNCTION IN HUMAN INFANTS. J.Martínek, M.Janovský, M.Chromá, V.Balíková. Inst. of Physiology, Czechoslovak Academy of Sciences, Frague, Czechoslovakia.

1107

In adult man and other mammals GFR does not significantly change even when the urine flow /V/ varies from antidiuresis to maximal water diuresis. In infants up to the age of 2.5 months GFR /inulin clearance/increased along with V: in a group of infants aged 0.5 - 1.5 months GFR was 25.0 ml/1/1.75 m² at an urine flow of 0.2 ml/1/1.75 m² and 75.0 ml at a V of 10.0 ml. The regression line of GFR vs. V was linear with an equation y= 28.38 + 4.72 X. In a group of infants aged 1.5 - 2.5 months GFR was 45.0 ml at V 0.2 ml and 85.0 ml at 10.0 ml. The equation of regression line was y= 44.57 + 4.17 X. In infants aged 2.5 - 4.5 months the relationship between GFR and V was changed to a logarithmic one with an equation y= 67.92 + 13.88 x logN X, i.e. the augmentation limit was similar to that in adults. In further regression analysis of the relations between V and osmolar clearances the phenomenon will be discussed from the point of view of comparative physiology.

1108 COMPARISON OF THE EFFECT OF PROSTAGLANDINS (PGE) AND ACETYLCHOLINE (Ach) ON RENAL SODIUM AND WATER EXCRETION. M. Martinez-Maldonado, N. Tsaparas, W. N. Suki and G. Eknoyan. Dept. of Med., Baylor College of Medicine and Veterans Administration Hospital, Houston, Texas,

Renal vasodilatation increases sodium excretion ($U_{Na}V$). PGE have vasodilating properties, are present in the kidney and may play a role in $U_{Na}V$ control. The vasodilating properties of Ach are well known. If solely due to vasodilatation, the renal actions of PGE and Ach should be similar. PGE and Ach were infused into one renal artery of hydropenic dogs (Group I); and dogs infused with hypertonic (Group II); isotonic (Group III); and hypotonic (Group IV) saline. PGE and Ach increased $U_{Na}V$ in Groups I and IV but not in Groups II and III. In Group I the relationship between free water reabsorption (T^{CH}_{20}) and osmolar clearance (C_{OSM}) was altered by both drugs: at any level of C_{OSM} , $T^{CH}_{20}V$ was less than control. Similar but smaller changes occurred in Group II. $T^{CH}_{20}V$ remained unchanged after Ach but was depressed by PGE in Group III. PGE and Ach increased urine flow (V) and free water clearance ($C^{CH}_{20}V$) in Group IV. The relationship $C^{CH}_{20}V$ to V remained unchanged with both PGE and Ach. These data indicate that both agents suppress proximal tubular reabsorption. The lack of alteration in sodium excretion in Groups II and III as compared to Group I indicates that the hemodynamic changes produced by Ach and PGE had already been achieved by the saline infusions. PGE must have diminished collecting duct water permeability since $T^{CH}_{20}V$ was reduced in Group III.

1109 EFFECTS OF THEOPHYLLINE AND IMIDAZOLE ON ADRENAL RESPONSES TO HORMONAL STIMULATION IN VIVO. J.Marton and K.Mihály. Department of Pathophysiology, Institute of Experimental Medicine, Hungarian Academy of Sciences, Budapest, Hungary.

Theophylline, an inhibitor of nucleotide 3;5' phosphodiesterase, was found to potentiate and imidazole, a phosphodiesterase activator, to inhibit the corticosterone secretion in response to ACTH in the hypophysectomized rat. Four consecutive daily doses of either theophylline or imidazole administered in combination with ACTH failed to affect adrenal growth. In intact animals subjected to acute stress imidazole prevented a rise in plasma corticosterone level within the first 20 minutes, but at 24 hours caused only partial inhibition. It is suggested that the synergistic action between ACTH and the nucleotide 3;5' phosphodiesterase inhibitor on the one hand, and the antagonistic action of an activator on the other, is additional evidence that adenosine 3;5'-monophosphate is an intracellular mediator of the steroidogenic action of ACTH.

1110 INTEROCULAR TRANSFER OF DELAYED RESPONSES IN NORMAL AND SPLIT-BRAIN ANIMALS. C.A. Marzi.Inst.of Physiology, University of Pisa, Pisa, Italy.

Normal cats and cats with section of the telencephalic and diencephalic commissures plus a midsagittal section of the quadrigeminal plate have been tested at several delays for intratrial interocular transfer of spatial delayed responses. Visual input was restricted to a single eye by using colour ed lights and corresponding colour filtres on contact lenses. On each trial the pre-delay cue was presented randomly to a single eye and the post-delay performance was tested when using either the same eye (monocular trials) or the other eye (transfer trials). Each session consisted of an equal number of trials in the two conditions. The ratio between the number of errors to criterion in the transfer and in the monocular trials was calculated for each subject. Performance of split-brain cats was not significantly different from that of normal animals, suggesting that interocular transfer of spatial cues does not require the removed structures. Transfer of non-spatial delayed responses is being tested at the present time. (Supported by Contratto C.N.R. 70.01687/18).

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VASCULAR REACTIVITY OF THE ISOLATED IN-VIVO PERFUSED DOG LUNG. W.H. Massion. Dept. of Physiology and Biophysics, Univ. of Oklahoma Med. Sch., Oklahoma City, Okla., USA

The pulmonary vascular response to E. coli endotoxin, epinephrine, histamine and angiotensin II was explored in the isolated, in vivo perfused lung lobe preparation of the spontaneously breathing dog. When heparinized blood perfused the lobe, addition of endotoxin was followed by an increase of pulmonary vascular resistance and blood volume with a fall in leukocytes and platelets. When the perfusing blood was anticoagulated with ACD (acid, citrate, dextrose) endotoxin produced leuko- and thrombocytopenia, but pulmonary resistance and blood volume remained unchanged. The response to endotoxin could be restored by administration of Ca⁺⁺ and heparin to the ACD preparation. Epinephrine, histamine and angiotensin II raised pulmonary vascular resistance regardless of the type of perfusate used. Lung lobes perfused with blood rendered leukopenic by passage through a leukocyte filter exhibited a high vascular resistance which increased further in response to endotoxin. It is concluded that the rise in pulmonary vascular resistance seen after injection of endotoxin is not due to mechanical obstruction of the vascular bed by leukocytes and platelets but may be related to humoral factors which require the availability of ionized Ca. (Supported in part by the John A. Hartford Fndn. and the Office of Naval Research Contract NO0014-68-A-0496)

1112

INFLUENCE OF INCREASED AND DIMINISHED FUNCTIONAL LOADING ON GROWTH AND DEVELOPMENT OF TABULAR AND PELVIC BONES OF ALBINO RATS IN THE PROCESS OF ONTOGENESIS. D.Mateeff, N.Bodourov, K.Binev, D.Yonkov, L.Cheresharov, S.Toshkova, R.Radomirov. Inst. of Physiol., Bulgarian Acad. of Sciences, Sofia, Bulgaria.

Comparative roentgenophotoosemetric measurements were made of the tubular and pelvic bones of control, immobilized and training albino rats, deisgned to ascertain the influence of movement on bone development and density. The results of the investigations show that functional loading with physical work leads to regular dynamic modifications in the length and thickness of the bones and the compact and in bone density. Immobilization of the rats results in inhibition and poor development of tubular bones and the bone system generally. In control rats the occurring modifications are less distinctly expressed, approximating in degree those of the immobilized rats.

1113

ON DNA CONTENT IN THE NUCLEI OF SPINAL CORD MOTONEURONS OF RATS UNDER REGIMENS OF FUNCTIONAL LOADING AND IMMOBILIZATION (CYTOPHOTOMETRIC STUDY).

D.Mateeff, E.Chakarov, Y.Tzacheva, K.Miteva, L.Cheresharov, D.Yonkov, R.
Radomirov, S.Toshkova. Inst.of Physiol., Bulgarian Acad.of Sciences,
Sofia, Chair of Histology and Embryology, Medical School, Varna, Bulgaria

A single-wave probe densitometry of nuclei of spinal cord motoneurons of albino rats, subjected to regimens of functional loading (treadmill exercise) and immobilization, was made on paraffin sections, stained after Feulgen. It was found that the amount of DNA in the nuclei of motoneurons of trained animals is greater than that of immobilized ones. The possible mechanisms are discussed for the occurrence of this difference.

CHANGES OF THE PROTEIN METABOLISM IN TRAINED AND IMMOBILIZED ALBINO RATS UPON PHYSICAL LOADING. Dr. Mateeff, M. Sheitanov, S. Radev, L. Cheresharov, D. Yonkov, R. Radomirov, S. Toshkova. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Studies were made on the rate of protein synthesis in the liver, kidney and heart in trained and immobilized albino rats during physical exercise and in different periods after termination of the exercise. In the controls as well as in the trained and immobilized rats the intensity of glycine-2-C incorporation during physical exercise was lowered. During the period of recuperation, the intensity of radioactive glycine incorporation was increased, for a given period it exceeded considerably the initial values - phase of exaltation, and about the 24th hr it became normal again. In the immobilized animals this reaction was delayed, no clearly manifested and at a much lower level as compared with the trained animals.

UPON SOME CONDITIONED REFLEX INDICES IMMOBILIZED WHITE RATS AND IN TRAIN-ED RATS. Dr. Mateev, N. Georgieva, L. Cheresharov, D. Yonkov, S. Toshkova, R. Radomirov. Inst. of Physiology, Bulgarian Acad. of Sciences. Centre of Gerontology and Geriatry, Sofia, Bulgaria.

In conditions of free behaviour the effect of different moving regimens upon proceeding of conditioned reflex reactions in senescent white rats were studied. Treadmill training in senescent animals drive to accelerated forming of conditioned reflex compared to that in immobilized animals. Latent periods of conditioned reactions in trained rats are significantly shorter, than these of the control animals. Actions of the high nervous system in senescent animals are positively influenced by the functional loading. Limitation of the movement drive to opposite effect - retarded forming and proceeding of the conditioned reflexes.

ALTERATIONS IN RECEPTOR BINDING OF 3H-ESTRADIOL PRODUCED BY CLOMIPHENE AND NEONATAL ANDRO-GENIZATION IN THE RAT. R. A. Maurer and D. E. Woolley, Dept. of Animal Physiol., Univ. of Calif., Davis, California, U.S.A. 95616

Levels of estradiol receptors in various tissues were estimated pharmacologically by determining the effects of clomiphene, which competitively blocks uptake of estradiol by specific receptors, on the distribution of radioactivity one hour after intravenous injection of 3H-estradiol. The results showed that uterus, anterior pituitary and anterior hypothalamus contain high concentrations of receptors. Posterior hypothalamus, prehypothalamic area, septum, and amygdala-periamygdaloid cortex also contain receptors, but in lower levels. Olfactory bulbs, hippocampus, brain stem, and cerebral cortex do not contain detectable receptor activity. Androgenization, produced by a single injection of testosterone propionate at 5 days of age, altered uptake of 3H-estradiol during adulthood. Androgenized rats and their litter mate controls were ovariectomized during adulthood and 2 days later the distribution of radioactivity after intravenous injection of 3H-estradiol was determined. Levels of radioactivity were less in uterus and anterior and posterior hypothalamus of animals treated neonatally with 100 µg testosterone than in control rats, whereas levels were not altered in pituitary, 5 brain areas, and peripheral nontarget tissues. Androgenization with 30 µg testosterone significantly reduced uptake of radioactivity only in anterior and posterior hypothalamus. Thus, androgenization affects receptors in some target tissues only. (Aided by an NIH fellowship to R.A.M. and by funds from NIH grant ES-00163 and the Health Sciences Advancement Award.)

FLUID TRANSPORT BY THE ENDOTHELIUM OF THE CORNEA. D.M. Maurice, Div. Ophthalmology, Stanford Medical School, Stanford, Cal., 94305, USA

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The normal thickness of the mammalian cornea is maintained by an active mechanism. This is shown by the excised tissue swelling when it is refrigerated and pumping the absorbed fluid out again on incubation. The process can be followed by measuring the thickness of the tissue under the microscope and occurs whether or not the epithelial layer is present; it appears therefore to be a function of the endothelial cell layer. By mounting the endothelian between two chambers fitted with capillary tubes, the fluid movement against a hydrostatic pressure gradient can be observed directly. The fluid flux amounts to 60 mm³/cm² hr and is not associated with an electrical potential over 0.5 mV. The movement is reversibly inhibited by low temperatures and anoxia, but not affected by 1 mM Fluoracetate or 0.2 mM Dinitrophenol.

SOCIAL SIGNALS IN SQUIRREL MONKEYS: ANALYSIS BY CEREBRAL RADIO STIMULATION. M. Maurus and D. Ploog. Max Planck Institute for Psychiatry, Munich, German Federal Republic.

1118

Social signals of squirrel monkeys (Saimiri sciureus) were elicited by remote-controlled brain stimulation. The method employed permits a study of signal-response interdependencies in varying social situations which can be chosen at the experimenter's will. The function of a signal and thereby its information content are largely determined by the response of the recipients. The analysis of signal function was attempted under five conditions of social interactions:(1) reactions of group members to attack behavior of the stimulated animal, (2) reactions to dominance gestures of the stimulated animal, (3) reactions to signals that are indiscernible to the human observer, (4) reactions that are unusual or abnormal, and (5) reactions to signals sent over greater or lesser distances. Several aspects of the signal proved to be decisive for the prediction of behavior: (1) the signal intensity, (2) the space between animals, and (3) the context. The control of these variables by means of radio stimulation permits further quantitative studies of signal characteristics and their effects on the modification of social behavior.

1119

EFFECT OF ATP AND OTHER PHOSPHORYLATED COMPOUNDS ON ACTIVE TRANSPORT OF PARA-AMINOHIPPURATE IN CORTICAL KIDNEY SLICES. J. Maxild. Inst. of Med. Biochemistry, University of Aarhus, 8000 Aarhus C, Denmark.

The uptake of p-aminohippurate (PAH) in thin cortex slices of rabbit kidneys, incubated in an oxygenated electrolyte medium, was studied under various conditions. Addition to the incubation medium of ATP (0.25 mM), ADP (0.75 mM), and AMP (1.5 mM) gave rise to a 50 % reduction of PAH accumulation. Moreover, UTP, CTP, GTP, TTP, and 3,5-cyclic AMP caused a pronounced inhibition of PAH uptake, whereas creatine-P had no effect. It was found that pre-incubation of the tissue with cyclic AMP increased the intracellular level of ATP with 63 %, but did not affect PAH accumulation. Addition of pyruvate, L-lactate, and acetate to the medium stimulated the accumulation of PAH about two-fold, while no significant effect on ATP concentration could be detected. PAH accumulation was much more reduced than the ATP concentration in the presence of "uncouplers" of the oxidative phosphorylation (2,4-DNP and CCCP). In contrast, oligomycin decreased PAH accumulation and ATP concentration to the same extent. It is suggested that active renal transport of PAH is intimately linked to the respiratory electron chain, but the transport mechanism presumably does not involve ATP (or other well-known energy-rich phosphate compounds) as an energy donor.

1120 CODING OF BACKGROUND ILLUMINATION BY PEAK FREQUENCY AND LATENCY OF RESPONSES OF RETINAL GANGLION CELLS. H.U.May and B.Fischer. Neurologische Universitätsklinik, Abteilung Neurophysiologie, Freiburg i.Br., Germany.

For information about stimulus flux A·I and background luminance I_0 from retinal ganglion cells knowledge on discharge frequency and stimulus onset is required. The latter is not contained in the retinal output. The maintained discharges of nearly all the neurons in the cat's retina are porly correlated with I_0 . Microelectrode recordings from ganglion cell axons and quantitative analyses of responses to stimulation of receptive field centers yield information about I_0 , against which the light spots of different luminance-to-threshold ratio I/I_s were presented: discharge frequency is an increasing function of I/I_s alone, whereas the peak latency I_0 , calculated from the post stimulus time histogram, decreases at constant I_0 . In addition I_0 decreases with increasing I_0 at constant I/I_s . Hence I_0 and discharge frequency together contain the information about $A \cdot I$ and I_0 . Retinal messages alone seem not to be sufficient to code I_0 as known from stabilized retinal images in men showing disappearance of pattern and brightness perception. Therefore it is assumed that additional information from other sources – for instance from eye movements and blinking – contributes to the perception of general brightness.

1121 REGULATION OF PHOSPHORYLASE ACTIVATION IN SKELETAL MUSCLE IN VIVO. S.E. Mayer and J.T. Stull. Univ. of Cal., San Diego; La Jolla, Cal., USA

Biochemical evidence indicates that the glycogenolytic response of skeletal muscle to catecholamines is mediated by cyclic 3',5' AMP (CA) through the stimulation of a protein kinase that catalyzes the transformation of nonactivated phosphorylase kinase (PK) to an activated form. This enzyme then catalyzes a Ca++ dependent conversion of phosphorylase (P) b to a. Regulation of P activation in rabbit gracilis muscle in vivo was investigated by measurements of CA concentration and PK and P activities 0-60 seconds after intra-arterial isoproterenol (Iso). Doses from 10^{-12} to 10^{-9} moles of the catecholamine stimulated P a formation in 3 phases: 1) P a formation without change in PK or CA; 2) P a formation correlated with increased CA and conversion of nonactivated PK to the activated form; 3) further P a formation with greater CA, but no greater formation of activated PK. β -blockade by 10^{-13} moles propranolol partially inhibited both CA and P a responses to Iso (10^{-10} moles) but not formation of activated PK. Propranolol (10^{-9} moles) completely inhibited all responses. Tetanic contractions alone rapidly stimulated Pactivation without any change in CA or PK, and did not alter CA or PK responses after Iso(10^{-10} moles). These results confirm that muscle contraction induces activation of P independently of CA and activated PK formation (Drummond et al. J. Biol. Chem. 244: 4235, 1969). They also suggest that the glycogenolytic response in skeletal muscle to a catecholamine involves regulation more complex than amplification through a simple cascade.

MODULATION OF TRANSMITTER RELEASE BY LOCAL PRESYNAPTIC POTENTIALS IN CRUSTACEAN NEURONS. <u>D.M.Maynard</u>. Dept. Biology, Univ. Oregon, Eugene, Ore. USA.

Inhibitory transmitter release by neurons in the lobster stomatogastric ganglion is potentiated by local, non-spike, depolarizing presynaptic potentials. Microelectrodes were placed in pre- and postsynaptic neurons. Unitary, monosynaptic IPSP in the postsynaptic unit followed presynaptic action potentials when the latter occurred spontaneously, were elicited by normal orthodromic input, or were evoked by depolarizing current applied through the presynaptic microelectrode. In contrast, antidromic action potentials in the presynaptic unit did not evoke postsynaptic IPSP unless combined with subthreshold depolarizing currents in the presynaptic element. In some neurons, subthreshold presynaptic depolarization alone was sufficient to release inhibitory transmitter and hyperpolarize the postsynaptic element. Indeed, action potentials were never observed in one class of such presynaptic neurons. The level of applied presynaptic depolarization necessary to cause significant transmitter release was comparable to depolarization caused by normal subthreshold synaptic input to the presynaptic element. We presume that chemically mediated neuron interaction may occur in neuropil without intervening action potentials. (Aided by NIH NS-09474)

OXYGEN AVAILABILITY OF HUMAN MYOCARDIUM RECORDED WITH CHRONIC ELECTRODES. H.Mazzella, O.Fiandra, C.H.Peluffo, E.Spera (Depto. de Fisiología, Facultad de Medicina, Montevideo, Uruguay.)

The oxygen availability (PO2) of the ventricle wall was measured in relative terms in 3 patiens with a polarographic technique (naked platinum or gold electrode). During surgery for repairing atrial or mitral defects the electrode, O.29 mm. diameter, was introduced 2-3 mm. beneath the epicardium of the left ventricle wall. Several days after operation the corresponding cable was connected to a D.C. O.7 volt power supply and a long Ag- Ag Cl2 electrode was introduced into the subcutaneous tissue of the left arm. Records were made on a Grass polygraph. Lead II of the ECG and sometimes the myocardial electrogram were also registered.— At rest, the myocardial PO2 was stable with small oscillations. Transitory increases of PO2 were provoked after inhalation of 100% O2 or CO2 5% in O2. A decrease of PO2 was seen during voluntay apnea, inhalation of 100% N2, Valsalva maneuver, or ocular compression. Amyl nitrite increased the myocardial PO2 in one experiment. compression. Amyl nitrite increased the myocardial PO_2 in one experiment. Movements of the legs also increased the PO_2 . The O_2 cathode continue to function by periods of 4-6 weeks. It was finally removed by slight traction under ECG and fluoroscopic control.

In summary, our results show that the oxygen electrode is valuable in the local study of human myocardial PO_2 .

A COMPARISON OF LONGITUDINAL AND CIRCULAR MUSCLE IN LARGE BOVINE MESENTERIC VEINS, T.A. McCalden, J.G. McConnell and L.C. Roddie. Department of Physiology, The Queen's University of Belfast. N. Ireland.

The pharmacology and innervation of vascular smooth muscle in bovine mesenteric veins was studied using isolated strips. Longitudinally cut strips showed rhythmic spontaneous activity and contracted strongly in response to electrical stimulation (E.S.), noradrenaline (NOR), acetylcholine (ACh) and 5-hydroxytryptamine (5-HT). Atropine significantly reduced the responses to ACh and E.S. without changing the response to NOR. Phentolamine significantly reduced the response to NOR, but not those to ACh or E.S. Circularly cut strips showed no spontaneous activity and contracted strongly to 5-HT, weakly to E.S. and NOR, and not at all to ACh. Atropine and phentolamine significantly reduced the response to E.S., but neither had any effect on the responses to 5-HT. is concluded that the longitudinal smooth muscle differs pharmacologically from the circular muscle. It is also concluded that the longitudinal muscle has a strong excitatory cholinergic innervation, while the circular muscle has a weak excitatory innervation involving ACh and NOR.

ENERGETICS OF SUPER-CONTRACTED SKELETAL MUSLCES. Med. Col. Va., Richmond, Va., U.S.A. Supported by NIH Grant 06389.

Isolated sartorius muscles of frogs were stimulated to shorten to average sarcomere lengths below 1.64. Repeated stimulation caused the muscles to pass into the delta state (as evidenced by the absence of relaxation and a 50% decrease in the maximum isometric tension). Once in this state, the muscles performed reproducible contractions over a period of 8 hours. The oxygen consumption was measured at 12 C using a modified Fenn respirometer. The steady rate of resting respiration was 40% higher than that of normal muscles and was not influenced by the length of the muscles. When the muscles were stimulated, the increased oxygen consumption was approximately the same under both isometric and isotonic conditions. This active consumption was 50% less than the value obtained for normal muscles performing isometric contractions (associated with the approximately 50% drop in performance). The mean maximal mechanical efficiency was 11.5 ± 1.5 (S.E.M., n 10)%. The results suggest that the normal energy transduction process remains intact in spite of the drastic structural alteration which accompanies the change into the super-contracted state.

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BIOCHEMICAL MANIPULATION OF THE RESPIRATORY FUNCTION OF BLOOD. Rita McConn and John B. Derrick. Einstein Col. of Med. and New York Blood Ctr., New York, N.Y. U.S.A.

Significant increases and decreases in P50 values were seen in serial studies of the oxygen dissociation curve of red blood cells whether from acutely-ill patients or blood stored at 4°C. The biochemical findings suggest that this dynamic character of the dissociation curve is, in both instances, a direct manifestation of changes in the intracellular environment. We have attempted by incubation experiments with acid-citrate-dextrose (ACD) blood stored for up to 20 days to delineate the common factors causing these changes. There were significant increases in 2,3 diphosphoglyceric acid (2,3 DPG) concentration, P50 values and a partial restoration of the ionic gradient when stored blood was incubated with inosine (10mM). A similar and more pronounced effect was seen by simply

tration, P50 values and a partial restoration of the ionic gradient when stored blood was incubated with inosine (10mM). A similar and more pronounced effect was seen by simply buffering the blood to pH 7.2 using ethanolamine. The CO2 tension also appeared to influence 2,3 DPG production. These observations indicate a non-Bohr role of pH and CO2 on the oxygen dissociation curve mediated through their effect on the metabolic regulation of 2,3 DPG production. This work indicates that reversal of unfavorable shifts in the dissociation curve i.e. lowered P50 requires restoration and/or maintenance of the normal milieu intérieur, a difficult accomplishment whether in the acutely-ill or stored blood. However a new approach to this problem is indicated by our studies which show that incubation of stored blood with methyl prednisolone (Solumedrol, Upjohn) effectively influences the restoration of 2,3 DPG and hence the P50 values. This suggests the possibility of manipulating the dissociation curve either in vitro or in vivo as a therapeutic modality. Supported by NIH Grants RR-00066 and HE 090TI.

1127 CIRCULATORY RESPONSE TO SINUSOIDAL VIBRATION AND THE EFFECTS OF HYPOVOLEMIA.

E. P. McCutcheon, R. G. Edwards, C. F. Knapp, and W. O. Griffen. Univ. of Kentucky Medical Center and Wenner-Gren Res. Lab., Lexington, Kentucky 40506, U.S.A.

Despite considerable recent interest, only limited direct experimental data are available which describe the cardiovascular response to environmentally produced accelerations. Flow velocities were recorded from transducers chronically implanted around the aorta, pulmonary, femoral, and carotid arteries and catheter-tip pressure gauges were used to simultaneously monitor arterial blood pressures. Six dogs and one pig were vertically restrained and exposed to whole-body (Z-axis) vibrations in the 2 to 12 Hz frequency range at acceleration amplitudes from 1 to 3 G, i.e. 980 to 2940 cm/sec². Compared to flow rates in the resting animal, flows occurring during low frequency vibration (frequencies close to that of the heart) can be increased by more than 100% or decreased to approximately zero for a given flow cycle in a major artery. To date, one dog has been vibrated before and after removing 42% of its blood volume. Similar results were recorded in the hypovolemic dog, even though the blood volume reduction reduced the peak aortic velocity by approximately 50%. The alterations were a function of (1) phase relationship between vibration motion and cardiac systole, (2) vibration-induced internal organ system motion, and (3) vibration frequency and acceleration intensity. (Supported in part by the Air Force Office of Scientific Research (AFSC), United States Air Force, Contract Number F44620-69-C-0127.)

IONIC INFLUENCES ON SPERM BIOPOTENTIALS. McGrady, Angele and Nelson, Leonard. Medical College of Ohio at Toledo, Toledo, Ohio, U. S. A.

Our investigations on the bioelectric characteristics of the sperm cell membrane and ionic movements indicate a significant role in the coordination of flagellar wave propagation. Washed sperm samples are suspended in Ca-free Ringer fructose phosphate containing 1.5% methylcellulose. Sperm heads are impaled with glass microelectrodes and recordings made with an oscilloscope through a high input impedance amplifier. The potential difference appears to be related to the degree of motility. An active cell has a resting potential of -10mv and a specific membrane resistance of 0.3 ohms/cm2 Reproducible periodic depolarizations are seen. Non-motile living cells have membrane potentials of -2mv and a lower resistance. In 3% methylcellulose, both fluctuations in potential and flagellar activity are suppressed. We believe that the physical constraints may inhibit triggering of the flagellar wave and so prevent depolarization because of the tight linkage between the conduction-contraction coupling. Reported effects of varying cation content on sperm motility have been corroborated by measurements on our cinephotomicrographs; when we increase the extracellular potassium 20 fold, the biopotential shifts in the direction of depolarization. Neither fixed charges nor mechanical vibration can by themselves account for alterations in bioelectrical parameters induced by modifications of sperm motility following changes in the viscosity or ionic imbalance of the medium. This work supported by USPHS Contract NIH 702313.

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EFFECTS OF ACUTE HYPOXIA ON BLOOD EXCESS LACTATE LEVELS IN ALTITUDE ACCLIMATIZED. James J. McGrath and Allan Abati. Rutgers University, New Brunswick, New Jersey, 08903 USA

The effect of acute hypoxic exposure on excess lactate production was studied in chickens hatched and raised at high altitude and in chickens hatched and raised at sea level. Male White Leghorn chickens, raised for one year at high altitude (12,500 feet) or for one year at sea level, were lightly restrained and placed in an exposure chamber. After a 2-hour equilibration period, the birds were exposed to a gas mixture of 10% 0_2 -balance N_2 for a period of 2 hours. Blood samples were withdrawn periodically from the unanesthetized birds before and during the hypoxic exposure by way of a carotid cannula. Respiration rates were monitored by means of a pneumograph. Excess lactate was calculated from levels of lactate and pyruvate found in the blood samples. Hyperventilation and mortality were greatest in the sea level birds. A rapid increase in excess lactate with subsequent leveling off after 30 minutes hypoxic exposure was observed for both altitude-acclimatized and sea level birds. Excess lactate concentration leveled off more rapidly and attained lower levels in the altitude birds.

1129

SLOW OUTWARD CURRENT IN VENTRICULAR MUSCLE. J.A.S. McGuigan. Inst. of Physiology, University of Berne, Switzerland.

1130

To voltage clamp small bundles of sheep or calf ventricular fibres (0.8 - 1mm diameter) both a single sucrose gap (Helv. physiol. pharmac. Acta 25, CR 189 - 190 1967) and a double sucrose gap have been used. Short clamps of 500 msec show no evidence of a time dependent increase in outward current, but when the clamp duration is increased to several seconds a slow increase in outward current is seen. Since the reversal potential of this current is around -60mV it is not a pure K current and it resembles the X currents described for Purkinje fibres (J. Physiol. 200, 205 - 231 1969). At potentials more positive than +30mV increasing the pulse duration shifts the measured reversal potential in a positive direction suggesting some effect of K accumulation; the effect of K accumulation at less positive potentials is not yet clear. Since a small, slowly increasing inward current (to diminish net outward current) prolongs the action potential it is suggested that this slow increase in outward current plays a part in repolarisation.

1131

THE CEREBRAL VASCULAR MECHANISMS PERTAINING TO THE "AUTOREGULATION". G.I.Mchedlishvili, N.P.Mitagvaria, L.S.Nikolaishvili, L.G.Ormotsadze, D.G.Baramidze. Institute of Physiology, Georgian Academy of Sciences, Tbilisi, U.S.S.R.

The resistance in the hemodynamically isolated internal carotid arteries of dogs was determined by recording of a set of hemodynamic parameters and by subsequent computing with an adequate mathematical model. The increase in the perfusion pressure produced with a pump was immediately followed by respective raise of the resistance in the internal carotid artery, thus, resulting in an absence or only insignificant changes of the blood pressure in the circle of Willis. This seems to be a substantial evidence indicating that the "autoregulation" seems to be a substantial evidence indicating that the "autoregulation" of the cerebral circulation is primarily brought about by the functional behaviour of the major arteries of the brain. When this mechanism is insufficient the pial arteries start to operate. However, their "autoregulatory" responses appear with a significant delay. The smaller arteries and arterioles located inside the cerebral cortex seem not to be involved in the mechanism of "autoregulation" of the cerebral circulation, e.g. under conditions of hypotension.

1132 METABOLIC AND NEUROHUMOURAL STUDIES WITH SUPERFUSED TISSUES FROM THE BRAIN. H. McIlwain, Dept. of Biochemistry, Inst. of Psychiatry, Univ. of London, England.

These experiments examined metabolic circumstances associated with uptake and release of noradrenaline, serotonin and amino acids (Baldessarini & Kopin; Srinivasan, Neal & Mitchell; Jones, Pull & McIlwain) in excised cerebral tissues incubated and superfused with Krebs-Ringer glucose-bicarbonate salines. In piriform- or neo-cortical tissues the two bases ($^3\mathrm{H}$ or $^{14}\mathrm{C}$ -labelled) reached concentrations 5-10 times those of the fluids, and of c.lnmole/g. Superfusion caused slow release, increased 3-10 fold in rate-constant during a few min. stimulation at 15 pulses/sec. This stimulation also increased 10-fold the lactate output of the tissue, which reached 3-4000nmoles/g.min.; loss of K⁺ and phosphocreatine were at initial rates of 2-3000nmoles/g.min. When lactate output was brought to high values by hypoxia (2-5% O2) little or no noradrenaline was released but electrical stimulation still released noradrenaline, with little additional lactate formation. Added Na glutamate also increased glycolysis without release of noradrenaline. Glutamate, glycine and other amino acids were released from the superfused tissue at a collective rate of c.60nmoles/g.min.; during some 20 min. superfusion the amount released exceeded the quantity of uncombined amino acid initially in the tissue. Release was nearly doubled by hypoxia and increased further by electrical stimulation. The different conditions had their greatest effects on the release of different compounds, and several parallels were found with cerebral events in vivo.

1133 ORGANIZATION OF HIPPOCAMPAL AND NEOSTRIATAL INHIBITION OF SOMATOSENSORY UNIT RESPONSES IN THE MEDIAL THALAMUS. J.S. McKenzie, D.K. Rogers, D.M. Gilbert. Dept. of Physiology, University of Melbourne, Victoria, Australia.

Hippocampal inhibition of medial thalamic unitary responses to limb stimulation was investigated in chloralose-anaesthetized cats, and compared with neostriatal inhibition affecting the same neurones. Concentric electrode stimulation of dorsal hippocampus or caudate nucleus, by single pulses or brief trains, inhibited responses only when applied to the hippocampal pyramids or to the dorsal shell of the caudate head. Most somatosensory units in the mid-zone of n. centralis lateralis were inhibited equally by prior stimulation of either hippocampus or neostriatum, at latencies from 5 to 30 msec., for durations of 250 to 500 msec. Inhibition by hippocampus only was concentrated in the rostral intralaminar area, and by caudate nucleus alone in the parafascicular complex, but some exceptions to this distribution trend were observed throughout the medial thalamus. Short-latency activation of medial thalamic somatosensory units, by central tegmental midbrain stimulation, was inhibited by hippocampus or neostriatum, implying a thalamic locus of inhibition but not excluding actions earlier in the somatic afferent pathway. Dorsal hippocampal effects were conducted via the fornix, but inhibition from the hippocampal gyrus appeared not to be mediated by the hippocampus. Inhibition of non-specific thalamic somatosensory responses provides a possible mechanism for the hippocampal control of conditional responding and attention, as inferred from behavioural data.

ANTRAL CONTROL OF GASTRIC ACID AND PEPSIN SECRETION IN THE SHEEP. L.M.McLeay and D.A.Titchen Sub-Dept. of Veterinary Physiology, Univ. of Melbourne, Parkville, Victoria, 3052, Australia.

There was a continuous secretion of acid and pepsin from separated innervated fundic pouches of the abomasum of sheep in which the entire pyloric antrum had also been made into a separated innervated pouch: the fundic pouch secretion of acid and pepsin of such animals increased on teasing with food, eating and irrigation of the antral pouches with isosmolal solutions containing 0.005% carbachol, 100 millimolar sodium acetate, sodium propionate and iso-butyric acid. Resting secretion of HCl and pepsin and the increases of them normally obtained on eating were reduced by irrigation of the antral pouch with 0.1% atropine sulphate, 1% hexamethonium bromide or HCl (pH 2.6 or less): during the reduction in secretion caused by antral irrigation with HCl or atropine the intravenous infusion of pentagastrin (1.2 ug/kg/hr) stimulated both acid and pepsin secretion. These experiments suggest the importance of the postganglionic cholinergic innervation of the antrum in the mediation of both the continuous secretion of the abomasum and its secretory responses on eating.

Aided by grants from the Melbourne Univ. Veterinary Res. Fund and the Australian Meat Res. Committee.

BILATERALLY EVOKED CENTRIFUGAL CUTAMEOUS NERVE DISCHARGES IN THE DECEREBRATE DECEREBRIATE

PHAIANGER, T. VULPECUIA. D. Megirian, Physiology Dept., Univ. Tasmania, Hobart, Australia It was previously reported that afferent volleys in coarse cutaneous fibers (A-alpha) of a hindlimb generate ipsilateral centrifugal cutaneous nerve discharges (CNDs) in fine cutaneous fibers (A-delta) after latencies of 30-35 msec (decorebrate-decerebellate preparation). The present study extends these observations to recordings made from contralateral cutaneous nerves and CNDs evoked bilaterally by vestibular nerve stimulation. Weak shocks applied to the latter elicited centrifugal CNDs recorded in both superficial peroneal nerves after equal latencies (35-40 msec) when recording electrodes were equidistant from the spinal cord. Retaining this recording arrangement, feeble shocks applied proximally to one superficial peroneal nerve provoked ipsilateral centrifugal CNDs after latencies of 30-35 msec whereas contralateral ones appeared after latencies of 50-55 msec. Conduction velocity determinations of centrifugal CNDs recorded in posterior extremities were uniform (19-24 m/sec) independent of whether causal afferent volleys originated in the labyrinth or the cutaneous nerve or whether such computations derived from recordings made ipsilateral or contralateral to the respective sources of afferent volleys. From these findings it is concluded that in the case of somatosensory stimulation the longer latency of centrifugal CNDs with respect to insilateral ones is due to an additional nuclear delay not found to be a feature of vestibular evoked centrifugal CNDs. (Supported, in part, by NS-07195 of the U.S. Public Health Service.)

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ETUDE MICROPHYSIOLOGIQUE COMPAREE DE L'INNERVATION AFFERENTE VAGALE ET SPLANCHNIQUE DU TUBE DIGESTIF. N. Meï, J. Crousillat, F. Raniéri.C.N.R.S., I.N.P. (Dept. Neurophysiologie végétative) - 13 MARSEILLE 9ème - France. 1136

L'innervation afférente du tube digestif est assurée par 2 groupes de neurones : les neurones vagaux et les neurones splanchniques qui demeurent encore peu connus. L'exploration par microélectrodes du ganglion plexiforme et des ganglions spinaux (T6 à L1) a permis de comparer l'origine et les propriétés de ces deux types de neurones. Dans l'oesophage, on trouve uniquement des récepteurs vagaux ; ils sont mis en jeu par la distension et la contraction et sont en rapport avec des fibres myélinisées de type B Le tractus gastro-intestinal contient en revanche les 2 sortes de fibres, mais leur distribution n'est pas partout identique. Dans l'estomac les fibres vagales comme les fibres splanchniques proviennent de mécanorécepteurs musculaires qui sont stimulés par la contraction et la distension ; elles sont myélinisées (type B) ou amyéliniques (type C). Dans l'intestin les fibres vagales prédominent nettement alors que les fibres splanchmiques innervent le mésentère. Les premières, qui sont exclusivement de type C, pro-viennent soit de mécanorécepteurs mis en jeu par le passage de l'onde péristaltique, soit de chémorécepteurs. Les secondes, de type B, sont issues de mécanorécepteurs sensibles au déplacement du tube digestif.

1137

INTERACTION BETWEEN STRONTIUM AND CALCIUM IONS IN TRANSMITTER RELEASE AT THE MOTOR MEAVE ENDINGS. U. Meiri and R. Hahamimoff. Dept. Physiol., Hebrew Univ. Med. Sch., Jerusalem, Israel.

The interaction between calcium and strontium ions on quantal transmitter release at the frog neuromuscular junction was studied, using conventional electrophysiological techniques. While calcium ions always activate transmitter release, the activating action of strontium ions depends on the calcium ion concentration in the medium; at low calcium concentration, strontium ions enhance the release, but at higher calcium concentration they inhibit it. Lhen strontium activates release, its effect and the effect of calcium add in a more than a linear fashion. The results can be explained by assuming that calcium and strontium act on the same site, at some stage of the process of quantal transmitter release. The affinity of both ions towards the sites is approximately the same, but the effectiveness of strontium is much smaller.

1138 EVIDENCE FOR THE THERMOREGULATORY SIGNIFICANCE OF THERMOGENESIS DUE TO ENDOGENOUS AND EXOGENOUS NORADRENALINE. J.Mejsnar, L.Jansky, S.Gregorová. Dept.of Comparative Physiology, Charles Univ., Prague, CSSR.

Infusion of noradrenaline in different doses (0,12 % - 1,10 % /100 g min) at thermoneutral zone elevates the metabolism of cold-adapted rats up to different quasistationary states, when an equilibrium between the supply of noradrenaline an its removal is achieved. Metabolic values during this equilibrium, plotted graphically with respect to infusion doses, in semilogarithmic scales, give a sigmoid dose-response curve. On the basis of this fact a smaller calorigenic effect due to a tested dose of noradrenaline in the cold than at thermoneutral zone indicates in our experiment an elevated concentration of endogenous noradrenaline in a cold and therefore the thermoregulatory significance of thermogenesis induced by noradrenaline. Doses of noradrenaline and the intensity of cold stimulus for the proof of the thermoregulatory significance of noradrenaline were estimated.

BRADYKININ-INDUCED LEUKOCYTOSIS AND PATHOGENETIC RELATIONSHIP OF THE VASOACTIVE NONAPEP-TIDE TO INFLAMMATORY AND INFECTIOUS PROCESSES. COUNTERACTION BY SALICYLATES AND CORTICO-STEROIDS. M. Mela, M.A. Balourdas and T.A. Balourdas. Inst. of Child Health at St. Sophia Childrens' Hosp., Athens, Greece and Hippocrates Med. Clinic, Cleveland, Ohio, U.S.A.

Functional and structural lesions in the microcirculation induced by synthetic Brady-kinin (BRS) were reported (Balourdas, T.A., Proc. IV Internat. Congress of Pharmacology, p. 382, July 1969, Basel, Switzerland, The Pharmacologist, 8:174, 1966, and the Physiologist, 10:133, 1967). The present investigations were undertaken to ascertain the role of participation of plasma kinins in the inflammatory and infectious processes and to detect the therapeutic counteraction of Salicylates and Corticosteroids. In a group of normal rats the blood leukocytes were counted before and after the I.M. injection of Bradykinin. Results: The treated animals with BRS exhibited an apparent leukocytosis 24 to 48 hours after the injection, the increase being over 42 percent. In the groups of animals with Salicylates and Cortisone before the administration of BRS there was found no leukocytosis, the leukocyte countings during the 24-48 hrs period being unchanged or slightly diminished. The beneficial effects of the anti-inflammatory agents are evident. The findings indicate the aspect of participating role of plasma kinins in inflammatory and infectious conditions with topical and systemic morbid manifestations. The mechanism of therapeutic effect of corticosteroids and salicylates may be due to the inhibition of the plasma kinins-forming enzymes. Beneficial effects of cortisone and ACTH were also observed on the whole-body irradiated animals with vascular damage, increased capillary permeability and hemorrhages.

1140 REDUCTION OF SUCKLING AND MILK REMOVAL IN THE RABBIT: EFFECT ON MILK SECRETION.

F. Mena, J. Pérez, G. Reyes and C.E. Grosvenor. Department of Physiology. Instituto de Investigaciones Biomédicas. Apartado Postal 70228. University of Mexico.

Mexico, D.F.

The amount of milk produced by one of the mammary glands of rabbits (New Zealand White) was reduced 20 to 30% when the rest of the glands were not suckled, as compared to a control situation in which all the glands were suckled. The observations were made on different rabbits on early (p.p. days 10 to 12), mid (p.p. days 12 to 22) and late lactation (p.p. days 22 to 30). Reduced milk yields lasted 2 days on either phase of lactation. After these 2 days, however, subsequent values varied according to the phase of lactation. Thus, on early lactation milk yields obtained after the 2-day milk yield reduced values, were above both, the 2-day reduced and the control values. On mid and late lactation, however, subsequent values remained at a lower level. Injections of 1 or 5 mg of ovine prolactin (NIH-P-S-9) on either phase of lactation restored milk yields to normal. These results suggest that the absence of suckling and milk removal of the mammary glands provokes a reduction of milk synthesis and that the capacity to compensate this reduction exists only during early lactation. The effectiveness of prolactin to restore reduced milk yields suggests that this hormone may be related with these effects.

MECHANISMS OF POSITIVE DORSAL ROOT POTENTIALS. Lorne Mendell, Dept. of Physiology, Duke Medical Center, Durham, N. C., U.S.A.

In high spinal cats stimulation of hindlimb muscle group III afferents results in

positive dorsal root potentials (DRP) at L6 with a central delay of 25 msec. These are depressed by barbiturate (20 mg/kg-IV). Test negative DRP's are inhibited during these positive DRP's; the inhibition is inversely proportional to the amplitude of the negative DRP with large negative DRP's showing no inhibition. This evidence does not support active hyperpolarization of presynaptic terminals as the basis for the positive DRP; it is suggested that the positive DRP results from inhibition of tonically active interneurons mediating the negative DRP. If a negative DRP is timed to occur during the steady negative DRP produced by 200/sec. stimulation of the tibial nerve, its amplitude and duration are diminished and it is followed by a positive DRP. The properties of this positive DRP are: a) a short central delay more characteristic of the negative DRP, b) insensitivity to barbiturate (20 mg/kg-IV), and c) facilitatory effect on a test negative DRP. It is suggested that this positive DRP results from removal of the steady negative DRP via presynaptic inhibition of the pathway producing the steady negative DRP. In conclusion 2 mechanisms for positive DRP's are proposed: a) inhibition of interneurons mediating the negative DRP; b) removal of excitatory drive from these interneurons. (Supported by NIH)

FURTHER STUDY ON THE REPLETION OF CLEARING FACTOR LIPASE (CFL) IN ISO-LATED PERFUSED RAT HEART. H. C. Meng and M. S. Ghosal, Dept. of Physiology, Vanderbilt University School of Medicine, Nashville, Tennessee, U.S.A.

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Heparin induces release of CFL from isolated perfused rat heart. The enzyme release is decreased when rats are injected with heparin 2 hours or less before perfusion. The maximal release of CFL occurs in 10 seconds; it is then reduced to a lower level despite continued perfusion. This low enzyme release is greater than the basal level from hearts perfused with a non-heparin medium and persists for a long period. The present study was to investigate the mechanism of "depletion" and "repletion" of CFL and its relationship to heart tissue lipase. The results are as follows: 1. Puromycin (100µg/ml) added to the heparin-containing perfusion fluid did not affect the CFL release. 2. CFL release from heparin-medium perfused hearts of normal rats and that from hearts of rats preinjected (4 hours before perfusion) with heparin showed no apparent difference. However, CFL release from hearts of heparin- and puromycin-pre-injected rats was reduced by 75% of that from hearts of rats given no puromycin. Puromycin injection also decreased the lipase activity of heart homogenates. 3. CFL release and tissue lipase were markedly decreased from hearts of rats given cycloheximide. It is proposed that there are two pools of CFL in the rat heart. The small pool is readily releasable and can be depleted. The second pool is large and requires synthesis for repletion. NIH grant 5RO1 HE-04372.

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THE EFFECT OF CRUSTACEAN EYESTALK EXTRACT ON RESPIRATION IN SELECTED MAMMALIAN TISSUES. William L. Mengebier, Department of Biology, Bridgewater College, Bridgewater, Virginia, and the Department of Zoology, University of New Hampshire, Durham, New Hampshire.

The effects of eyestalk extracts prepared from the crayfish, Cambarus bartoni, and the lobster, Homarus americanus, on endogenous and respiratory enzyme activity of selected organ homogenates of the rat and mouse were investigated. Extracts were prepared by homogenization in 0.1 M phosphate buffer, followed by centrifugation at 0°C for 180 minutes at 10,000 x g; Supernatants showed no respiratory activity. Addition of supernatants obtained from Cambarus bartoni, significantly increased the endogenous oxygen uptake of 10% liver, kidney, and brain homogenates of the rat; significant increases in the oxygen uptake of 10% mouse kidney and brain homogenates treated with Homarus americanus extract were also noted, but there was no increase in the activity of mouse liver homogenates similarly treated. Significant increases in the activity of the succinoxidase and cytochrome oxidase systems in rat brain treated with crayfish extract were recorded. The stimulatory effect of crayfish extract was unaltered by either dialysis for 48 hours or freezing for a maximum of two weeks. Boiling for 10 minutes destroyed all effects. Concentration of the crayfish extract with LYPHOGEL resulted in an increased stimulatory effect; in terms of the absorptive qualities of this gel, the active component(s) of the extract has a molecular weight above 24,000. Disc electrophoresis and staining with analine blue-black showed two distinct bands.

PULMONARY AND COLLATERAL FLOW RESISTANCE IN DOGS. H. Menkes, D. Lindsay, G. Gamsu,
L. Wood, A. Muir and P.T. Macklem, Respiratory Division, Royal Victoria Hospital,
Montreal, Quebec, Canada.

We compared pulmonary resistance (R_L) and collateral resistance (Rcoll) in anesthetized, paralyzed dogs. We also measured Rcoll in isolated lungs from freshly exanguinated dogs. R, was measured with a forced oscillation technique and Rcoll was measured by injecting air through a double lumen catheter wedged in a bronchus. The volume of the lung (V_L) was measured with a plethysmograph. The volume of the segment distal to the wedged catheter (V_S) was measured in two ways. First, the volume of air leaving the segment during a slow deflation of the whole lung was estimated using the collateral channels as a flowmeter. Secondly, a viscous mixture was injected into the segment, the lung was dried in air and the segment excised. The second method gave results which were 4.0 (SD 16.9) % higher. In 7 intact dogs, specific pulmonary resistance ($SR_L = R_L \times V_L$) and specific collateral resistance ($SRcoll = Rcoll \times V_S$) were compared. At transpulmonary pressures of 10 cm H_2O (P_LO), SRcoll was 9.91 (SD 8.79) cm H_2O sec. The ratio $SRcoll/SR_L$ rose from 7.10 (SD 5.06) at P_LO to 19.0 (SD 15.3) at FRC. In 7 isolated lungs, SRcoll was 2.72 (SD 1.46) cm H_2O sec at lung volumes comparable to those in intact animals at P_LO . We conclude that resistance to flow through collateral channels of segments occupying 1.1% (range 0.41 to 2.1) of the lung is much higher than the resistance to flow through airways. This difference is greater at lower lung volumes. In addition, it appears that Rcoll is higher in intact animals than in isolated lungs.

RELATIONS BETWEEN NEURAL DRIVE AND MECHANICAL RESPONSE IN THE VESTIBULO-OCULAR SYSTEM.

D. Mergler-Racine. Aviation Medical Research Unit, Physiology Dept., McGill University, Montréal, Canada.

It has been shown previously that the action potential frequency (APF) in the afferent limb of the vestibulo-ocular reflex tends to retain the angular velocity transduction to be expected from semi-circular canal hydrodynamics. This investigation studied the corresponding response in the efferent limb of this reflex. The 6th nerve of cats was exposed ventrally keeping the preparation intact. The level of anaesthesia was varied to completely eliminate eye movement, or to produce only smooth compensatory eye movement, or to produce a mixed smooth pursuit and saccadic movements (nystagmus). Motor unit activity, recorded from single fibres and multiple fibre bundles was related to horizontal eye movement, monitored by D.C. electro-oculography, during horizontal rotational oscillation of the animal. It was found that a) in the absence of "saccadic" eye movement, the APF of the 6th nerve displayed the same characteristics as those observed in the vestibular nucleus, and generated a proportionate angular velocity of compensatory eye movement and b) in the presence of saccades, the APF of the 6th nerve was no longer related to eye angular velocity in a simple way. Thus, the saccadic event changed the relationship between the neural signal and the mechanical response.

This research was supported by Canadian DRB grants: 9910-37 and 9310-92.

1146 RESPIRATORY MOVEMENTS IN FETAL LAMBS AND RABBITS IN UTERO. C. Merlet, J. Hoerter and C. Tchobroutsky, Lab. C.N.R.S., Hosp. Broussais, Paris XIVe, FRANCE.

It is generally admitted that the fetus in utero does not make rythmic respiratory movements providing it is not disturbed by asphyxia or any other stimuli. This conclusion was mainly drawn from acute experiments. A chronic preparation provides a long period of observation in an unstressed animal. Catheters were inserted into the fetal lambcarotid artery, trachea and/or oesophagus and the amniotic cavity between day 110 and 134 of gestation. Continous records were done. In all cases, intermittent periods of respiratory movements were observed, they represent approximately 50% of the observation time. Carotid blood gas values and pH are not significantly different in periods of apnea and of respiratory movements. The tracheal fluid flow is 185 ± 12 ml per day. In rabbit fetuses from day 28 to birth the same pattern of respiratory movements was observed using an indwelling pleural catheter.

EFFECTS OF PROSTAGLANDIN A₁ ON THE RAT MICROCIRCULATION. <u>E. J. Messina, R. Weiner, and G. Kaley</u>. Department of Physiology, New York Medical College, New York, N.Y. USA.

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Recent reports have implicated prostaglandins in the regulation of blood pressure and blood flow. The present investigation was carried out to characterize the vasomotor activity of prostaglandin A_1 (PGA1) on the microvasculature of the mesocecum and skeletal muscle (cremaster) of the rat. In vivo changes in microvascular diameters in response to PGA1 and selected vasoconstrictor agents were determined quantitatively by utilizing a microscope equipped with an image-shearing eyepiece in series with a television recording system. Topical administration of PGA1, in doses of 0.1 - 10 μg , produced a dose-dependent vasodilation of arterioles in the cremaster muscle. In contrast to the actions of prostaglandin E1 in the mesenteric microvasculature, PGA1 did not consistently dilate mesenteric arterioles, nor did PGA1 alter microvascular reactivity to locally applied angiotensin, epinephrine, norepinephrine and vasopressin in the mesentery and cremaster muscle. The observations cited suggest that prostaglandins A1 and E1 produce arteriolar dilation through different pathways. (Supported by USPHS, NIH Grants HE 12342 and GM 42317).

THE EFFECT OF SOMATIC AND VISCERAL INTERACTIONS ON THE RECOVERY PERIOD OF EVOKED POPENTIALS. I. Mészáros and E.S. Moniava. Eötvös Loránd Univ., Dept. of Comparative Physiology, Budapest, Hungary and Inst. of Physiology, Georgian Academy of Sciences, Tbilisi, USSR.

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The mutual effect of somatic /sciatic and radial/ and visceral /splanchmic/ afferent impulses has been investigated on anestethized and curarized cats in acute experiments by evaluating the amplitude of evoked potentials recorded from different structures of the brain /somatosensory and associative cortex, VPL and midbrain reticular formation/. Marked decrease of the amplitude of splanchnic responses has been observed 1,0 sec following the somatic stimulus, whereas 0,8-1,0 sec after the splanchmic stimulus, sciatic or radial evoked potentials showed significant facilitation. Applying the latter sequence of stimuli and diminishing gradually the interstimulus interval, the somatic response could be observed even in case of delay less than 50 msec. On the basis of the data the interrelations of visceral and somatic afferent systems are debated.

A New Multi-Microelectrode For Three-Dimensional Registration Of Tissue-PO2.* H. METZGER and W. ERDMANN. Departments of Physiology and Anesthesiology, 65 Mainz, German Fed. Rep.

1149

A new method described by ERDMANN, METZGER, KRELL, and NIXDORF (1970) permits the construction of glass insulated gold wires of 1 - 5 microns in diameter. These gold wires are the basis for a new multielectrode system. Six microelectrode tips of 1 - 5 microns in diameter are arranged equidistant on the corners of a hexagon. The base is a glass capillary of 50 microns in diameter with a seventh microelectrode tip centrally located. Thus, distances between the seven electrode tips are equally 25 microns. For reason of mechanical stability the extended free length of the electrode tips is limited to 1 mm. The reference electrode is fixed on the glass capillary in a thin layer form of conductible silver lacquer. A 6-channel polarographic system permits the registration of the PO2-gradient pattern and when moving the electrode forward a three-dimensional registration in a tissue cylinder of 50 microns. The electronic equipment of the seventh channel is designed for simultaneous PO2- and action potential measurement according to the method described by METZGER, KUNKE, and ERDMANN (1970). References: ERDMANN, W., METZGER, H., KRELL, W., NIXDORF, I.: Pfl.Arch. 319, R 69 (1970). METZGER, H., KUNKE, ST., ERDMANN, W.: Pfl. Arch. 319, R 68 (1970). *Supported by the Deutsche Forschungsgemeinschaft

THE RELATION OF THE 24-HOUR RHYTHM OF CARDIAC GLYCOGEN OF THE RAT TO RESISTANCE TO ASPHYXIA. D.K. Meyer. Dept. of Physiol., Univ. of Missouri Sch. of Med., Columbia, Mo., USA.

Male albino rats (Wistar) of 450-600 gm. wt. maintained in a controlled environment with a 12:12 light:dark cycle have a 24-hour rhythm of cardiac glycogen. In this series the high value of 6.68 mg/g of wet weight occurred 2 hours after the lights came on and the low value of 3.43 mg/g came 2 hours after the lights went off. This study was designed to assess whether or not the higher glycogen actually increased survival time of anesthetized rats subjected to asphyxia by clamping the trachea. Carotid blood pressure and the EKG were recorded. Five different stages in asphyxial death were timed: cessation of respiration, peak of blood pressure rise, a mean blood pressure of 50 mm Hg, 0 mm Hg blood pressure and failure of electrical activity of the heart. There is a significant increase in the time taken to reach the last 3 stages of asphyxial death in the high cardiac glycogen rats. It took 14% longer time to reach 50 mm Hg mean B.P., 32% longer to reach 0 mm Hg B.P. and 36% longer for failure of electrical activity of the heart. The rate of glycogenolysis is a function of the initial glycogen level. Therefore the increased survival time of the high glycogen rats is not directly proportional to myocardial level. The 24-hour rhythm of cardiac glycogen suggests that the role of glycogen is more than serving as an anaerobic metabolic reserve. Supported by NIH grant HE-07118.

1151 ACTIVITY PATTERNS IN THE OPTIC TECTUM DUE TO FLICKER STIMULATION. D.L.Meyer. Psychiat. Klinik Univ. Göttingen, Germany.

Responses of units to flicker stimulation have been investigated in different layers of the goldfish' optic tectum. Flicker was used with equally long on-off durations. Inhibitory phenomena, depending on flicker frequency are especially pointed out. Several units were tested under different temperature conditions. The effect of cooling on the responsiveness of tectal units is illustrated and compared with PROSSER's findings.

1152 CEREBRAL BLOOD FLOW BY TWO METHODS. M. Meyer, A. Klassen and J. Resch. Depts. of Physiology and Neurology, Univ. of Minnesota, Minneapolis, Minn., USA.

External isotope monitoring (I) and the particle distribution (II) methods assessed cerebral blood flow (CBF) in dogs. A gamma probe was positioned on the skull after reflecting the temporal muscle to obtain a clearance curve (CC) for Xe-133 injected in the ipsilateral carotid artery. Two CCs were recorded, one prior and one after left ventricular injection of labeled microspheres for II. To justify comparison of I and II, tissues essentially being observed by the probe were sampled for fractional uptake of spheres. Cardiac outputs were determined in II to calculate flow (F)/gm of cranial bone (Fb), gray (Fg) and white (Fw) matter, and of a mixed sample from the opposite hemisphere (F). A mean F calculated from Fg and Fw using a 60:40 gray to white ratio averaged 0.48 (ml/min·g) compared to an average \overline{F} of 0.50. Exponential analysis of CCs by computer usually yielded 3 exponential constants (α , β , γ). The largest (α) appeared to represent vascular transit of Xe. Fg/ β and Fw/ γ (estimates for Xepartition coefficients - λ g and λ w) averaged 0.98 and 3.4. A 3.4 λ w value is not realistic suggesting γ may be strongly influenced by Fb. β_1 and β_2 for CC₁ and CC₂ were similar if arterial pCO₂ remained constant, suggesting that spheres did not alter CBF. (Supported by USPHS Grant #s NB 03364 and DE 02212).

RENSHAW CELL ACTIVITY AND MONOAMINE LIBERATION, J. Meyer-Lohmann, C. Hellweg, R. Hagenah and R. Benecke. Dept. of Physiology, II, Univ. of Goettingen, Goettingen, German Fed. Rep.

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The influences of catecholamines and tryptamines upon the activity of Renshaw cells in the lumbosacral cord is investigated by conventional microtechniques in lightly anaesthetized (urethane-chloralose or viadril) or unanaesthetized decerebrate or acute spinalized cats. L-3,4-dihydroxyphenylalanine (DOPA 100 mg/kg i.v.), precursor of the catesholamines dopamine, adrenaline and noradrenaline, decreases the activity of Renshaw cells, induced by antidromic stimulation of muscle nerves, in the "intact" lightly anaesthetized cat, especially after pretreatment with reserpine (3-5 mg/kg i.p. 12-20 h previously). This and other results from decerebrate and spinal cats suggest that as far as DOPA influences the Renshaw cell activity, this will occur through the formation and liberation of dopamine, not of noradrenaline. By DL-5-hydroxytryptophan (5-HTP, 50-100 mg/kg i.v.), precursor of 5-hydroxytryptamine (5-HT), marked increases are seen in the background activity and responsiveness of the Renshaw cells to stimulation of muscle afferents, without alteration of their antidromically induced activity. It is not yet settled how far the effects of 5-HTP via 5-HT upon the Renshaw cells are secondary to an enhanced activity of alpha motoneurones.

RECEPTIVE FIELD ANALYSIS OF VISUAL-OCULOMOTOR INTERACTIONS. Joel A. Michael, Rush Presby-

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terian-St. Luke's Medical Center, Chicago, Illinois, U.S.A. 60612.

Proper processing of the ever-changing retinal image requires that the visual system be informed of the occurrence of internally generated eye movements. Previous single-neuron studies of such visual-oculomotor (V-O) interactions have yielded contradictory results; the lateral geniculate (LGB) and the visual cortex have been claimed and denied to be the site of such interactions. These contradictions may be the product of the different techniques employed to study single-neuron responses in the visual system. Arguments will be presented to support the claim that an examination of receptive field organization is required to determine the occurrence of V-O interactions; studies restricted to an examination of only the temporal firing pattern of visual system neurons, although of value, can not definitively establish the presence or absence of V-O interactions. Experiments have been carried out on encephale isole cats, with single neurons being monitored in a conventional manner in the LGB and visual cortex. A computer-based system employing a display CRT as a visual stimulator was used to calculate post-stimulus time histograms (PSHs) and receptive field maps. Oculomotor activity was induced by stimulation of the vestibular system. The results support the contention that information about receptive field organization makes possible a more meaningful assessment of changes occurring to visual processing mechanisms than does information about the PSH. Further, and more specifically, the results suggest a cortical site for visual-oculomotor interactions. This research was supported by Grant No. EY00567, National Eye Institute, USPHS.

MEASUREMENT OF PERMEABILITY OF SINGLE CAPILLARIES OF FROG MESENTERY TO DYES. C.C. Michel and J.R. Levick . Univ. Lab. Physiology, Oxford, England

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When a transilluminated capillary is perfused via a micropipette with a dye solution of known concentration, the changes in optical density resulting from the presence of dye in a section of the vessel and the surrounding tissues may be used to calculate capillary permeability to the dye. A step increase in optical density occurs as the dye fills the vessel lumen and this is followed by a slower progressive rise in optical density accompanying the accumulation of the dye in the tissues. When the slower rate of rise of optical density is extrapolated back to its initial value, it corresponds to the efflux of dye from the capillary when the tissue concentration of the dye is zero. Using appropriate calibration factors, both the initial efflux of dye and its initial concentration in the capillary may be calculated from the optical density. Assuming the capillary to be circular in cross section, the area of capillary wall may be determined and the capillary permeability (defined as flux/unit area/concentration gradient) to the dye may be calculated.

*M.R.C. Scholar

ATP-DRIVEN TRANSPORT BY FROG STOMACH DURING ANOXIA. Fabian Michelangeli, Ann B. Kircher, Anna Nickel and Richard P. Durbin. Cardiovascular Res. Institute, Univ. of California School of Medicine, San Francisco, California, U.S.A.

A positive correlation between acid secretion and ATP produced by stomach would support the hypothesis that ATP is an intermediate in the secretory process. Such a correlation was looked for in the present study by using 2-deoxy-D-glucose (2-DG) to inhibit anaerobic glycolysis. In paired experiments, secretion was stimulated with 10-4 M histamine; in one half of each pair, 2-DG (10 or 20 mM) was added to the serosal solution 1 hour prior to anoxia. Acid secretion, short-circuit current and lactate production were measured during the period from 20 to 60 minutes after initiation of anoxia. 2-DG lowered acid secretion from 802 (control) to 483 mymoles (p <0.05); short-circuit current, from 492 (control) to 215 mymoles (p <0.10); lactate production, from 618 (control) to 342 mymoles (p <0.001). From these values, and tissue levels of ATP and creatine phosphate, the molar ratio of acid secreted to ATP consumed was calculated to be 0.73 for control experiments and 0.78 in the presence of 2-DG. In other experiments, histamine was excluded from the solutions to obtain "resting" mucosae; acid secretion and lactate production during anoxia were significantly less than in stimulated mucosae (p <0.025). From these results, we conclude that active transport by the stomach during anoxia utilizes ATP supplied by glycolysis; ATP is therefore likely to be an intermediate in the normal secretory process. (Supported by NHLI Program Project Grant No. HE-06285).

1157 A BIOCHEMICAL BASIS FOR SODIUM APPETITE. A.R.Michell. Rockefeller Univ., New York, N.Y., U.S.A.

Despite sustained interest in salt appetite and the assumption that it may be important in the regulation of body fluids, there has been little examination of the concept of 'sodium requirement', that is, of what might signal a physiological need for augmented sodium intake. Partly this results from efforts to link sodium intake to sodium 'status' alone. Evidence in rats and in sheep, however, suggests that sodium appetite is also influenced by potassium status and led to the hypothesis that sodium appetite is governed by the rate of active transport of sodium and potassium in a yet undefined locus. Sodium appetite is enhanced when the rate of active transport of sodium is increased. Such a hypothesis can explain several of the anomalous observations in the field of salt appetite. It also leads to the prediction that while cardiac glycosides (which inhibit sodium transport) are likely to cause, if anything, negative sodium balance, they will nevertheless depress sodium appetite. Classically, negative sodium balance stimulates sodium intake. Results obtained in rats of both sexes show that digitoxin depressed sodium preference and intake whether given orally or intragastrically whereas it had no such effect on saccharin preference, a test both for another taste quality and for 'bait shyness'. The hypothesis seems, therefore, worthy of further investigation by extending the above studies, testing its other predictions, and perhaps by using cardiac glycosides to attempt to define a site where the biochemical process of electrolyte transport is translated into the behaviour of sodium intake.

1158 FREQUENCY DISCRIMINATION IN THE LOCUST EAR: BASED ON SELECTIVE RESONANCES.

Axel Michelsen, Zoological Laboratory, University of Copenhagen, Denmark.

Theories of selective resonances as the basis for frequency discrimination (f.d.) in the mammalian ear have been debated for more than a hundred years. Recently, an invertebrate preparation, the ear of the locust, has been found capable of f.d. The f.d. appears to be based on selective resonances in an inhomogeneous membrane, to which the receptor cells attach. The vibrations have been studied with laser holography and capacitance measurements. Two sets of mutually interfering resonances have been found. The spatial concentration and position of these resonances change with frequency. The vibration of the receptor cells' area of attachment is a maximum at their characteristic frequencies. The f.d. thus appears to be based only on the anatomical position of the cells and on the physics of the membrane.

ON THE INFLUENCE OF SEROTONIN ON THE METABOLISM OF HISTAMINE IN SOME ORGANS OF RABBITS. E. Miętkiewski, W. Mizgiert and B. Kośmicki. Department of Physiology, School of Medicine, Szczecin, Poland.

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In order to know better how histamine participates in shock mechanism, its level, formation and decomposition are simultaneously studied during various experimental shocks. Histamine metabolism, known to be dependent on e.g. stress factors or catecholamins, could also change under influence of larger serotonin doses. To elucidate that problem, serotonin was injected intravenously to 12 rabbits in doses each 3 mg/kg, whereupon they were sacrificed in groups of 3 animals after the following lapse of time: 5 min. - group I, 3 hours - group II, 6 hrs. - group III and 24 hrs. - group IV. Group V consisted of control animals which obtained serotonin solvent alone - 0,9 % NaCl solution. In studies for histamine level /H/, for its formation rate-histidine decarboxylase activity /HD/ and for decomposition rate-diamino oxydase activity /DAO/ were employed: blood, heart, lungs, duodenum, liver, kidneys and the spleen. Histamine level /H/ increased first in group I, but it diminished most distinctly in group II, wherein the histamine formation /HD/ was also diminishing most visibly, while the rate of its decomposition /DAO/ increased.

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CHANGES OF PHOTICALLY EVOKED POTENTIALS IN THE LATERAL GENICULATE BODY OF MONKEYS DURING RETROGRADE DEGENERATION.Lj.T.Mihailović, B.Beleslin, D.Cupić and N.Dekleva.Inst.of Pathological Physiology, Fac.of Med.Beograd, Yugoslavia. Rhesus monkeys were used. The bone flap over the left occipital region was turned on under anaesthesia and reimpacted into its original position.Bipolar, stainless steel electrodes were introduced in the lateral geniculate body(LGB) of both sides of the brain. Control recordings were taken a week thereafter. The animals were then reanaesthetized and subjected to a radical unilateral occipital lobectomy. Potentials evoked by flashes were recorded under standardized conditions up to 6 months. After an initial increase (between 12th and 72th post-operative hours)in both LGBs, more conspicuous in that of the operated side, the amplitudes of both main waves (A and B) returned to control levels within circa 10 days and remained almost unchanged until the end of the 1oth post-operative week. Then, another transient potentiation of the amplitude occurred and was followed by a gradual reduction until ultimate and irreversible disappearance of evoked potentials in the degenerated LGB ensued. In the LGB of the unoperated side, the amplitudes of evoked potentials fluctuated slightly around the control values. The electrophysiological changes have been interpreted with regard to numerical estimates of the degenerated neurons at the corresponding post-operative time intervals.

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INFLUENCE OF THE PARAMETERS OF THE VAGAL AFFERENT STIMULATION ON THE BLOOD PRESSURE. S. Mileva, V. Pavlov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

The investigations were carried out on cats under the conditions of acute experiment with chloralose anaesthesia and bilateral vagotomy. Variations were made in the amplitude, frequency and duration of the electric pulses with which n. vagus was stimulated. It was established that the stimulation of the central stump of n. vagus in the region of the neck invariably causes a fall in the systemic blood pressure. The different amplitude, frequency and duration of the pulses alter only the extent of the depressor reaction without affecting its pattern. Maximum fall of the blood pressure is obtained upon stimulation of n. vagus with a pulse amplitude of about 5.0 V, frequency of 20 to 30 pulses/sec and duration of the individual pulse of 3 msec.

1162 Na* REABSORPTION IN AN ISOLATED RABBIT KIDNEY PERFUSED WITH BLOOD AT DIFFERENT PLASMA PROTEIN CONCENTRATION. E. Milla and G. Torelli. Inst. of Gen. Physiol., Univ. of Milan, Milan, Italy.

In previous experiments it was shown that the total amount of readsorbed Na⁺ was decreased by lowering the blood protein concentration. These results weemed to be consistent with the hypothesis that an appreciable amount of Na⁺ could be passively reabsorbed owing to the blood colloid osmotic pressure. Present experiments on isolated rabbit kidneys perfused with blood to which liophylized rabbit plasma proteins were added, complete the previous ones. The total amount of reabsorbed Na⁺ was compared among experiments performed at three levels of protein concentration (4.0±0.1; 6.24±0.6; 8.91±0.18) and grouped according to classes of clearance values (10-20; 20-30; 30-40 ml g⁻¹h⁻¹). A significant increase of the total reabsorbed Na⁺ was found in each class of experiments by increasing protein concentration. These results give a further support to the importance of the colloid osmotic pressure in the process of Na⁺ reabsorption in the isolated rabbit kidney.

MYOCARDIAL FFA AND GLUCOSE METABOLISM IN THE UNANESTHETIZED DOG. H.I Miller and B.C. 1163 Durham. Div. of Research, Lankenau Hospital, Philadelphia, Pa., U.S.A. 19151

Myocardial free fatty acid (FFA) and glucose metabolism were studied in unanesthetized dogs at various plasma FFA levels. Exercise and norepinephrine (NE) infusion was used to raise FFA level while glucose infusion was used to lower it. Correlation between FFA level and myocardial uptake at rest was confirmed. A correlation between myocardial FFA removal and oxidation was found at rest, during exercise and during 10% glucose infusion. Isotopic palmitic acid and glucose were used to determine oxidation of these substrates in heart muscle. There was no difference between arterial and coronary sinus FFA or glucose specific activity. NE, while increasing FFA level greatly, increased myocardial FFA oxidation only moderately and decreased glucose oxidation to undetectable quantities. Plasma FFA accounted for 35% of the myocardial oxygen consumption at rest while glucose accounted for some 7%. During exercise, myocardial O2 consumption from glucose did not differ from rest (7%) but FFA rose to 75%, while 10% glucose infusion decreased FFA myocardial O2 consumption to 26% and increased glucose myocardial O2 consumption to 22%. Lactic acid was taken up by the heart at rest, during exercise and 10% glucose infusion. NE infusion caused a decrease in this uptake and in some cases appeared as an output. Myocardial arteriovenous triglyceride differences were very small, fluctuating between aptake and output and no definite trend was seen. At rest, the myocardium appeared to oxidize virtually 100% of the FFA extracted from the plasma, while during exercise there was an indication that more fatty acid was oxidized than was taken up. (Supported in part by USPHS, NIH Grants HE12636 & FR5585)

1164 CARDIAC NEUROPHYSIOLOGY OF THE AMERICAN COCKROACH. T. Miller. Dept. of Entomology, University of California, Riverside, California, 92502, USA.

The cardiac nervous system of the American Cockroach, Periplaneta americana L., consists of intrinsic neurons plus innervating axons from the central nervous system which together comprise paired lateral cardiac nervecords. There are two identified types of intrinsic cardiac neuron in the cardiac nervous system. One type gives rise to regular motor impulses with a conduction velocity of 0.5 M/sec. which innervate the myocardium and communicate with distal portions of the cardiac nervous system. The activity of these intrinsic motor neurons is correlated with postsynaptic potentials in adjacent myocardial cells. A second type of neuron in the cardiac nervous system is characterized by the presence of electron dense granules in the cytoplasm and is associated with nervous impulses whose conduction velocity is 0.2 M/sec. The two distinct cardiac neurons are each chemically sensitive to an individual range of organic compounds and one or the other or both can be activated by perfusion with the appropriate chemical.

THE ROLE OF ADENYL CYCLASE IN VISUAL EXCITATION. W. H. Miller, M. W. Bitensky, R. E. Gorman and A. H. Neufeld. Yale University Medical School, New Haven, Conn. 06510, USA.

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The rod outer segments of the frog retina contain an adenyl cyclase system that is active in darkness and inactivated by light. The action spectrum is that of rhodopsin. This cyclase system has a specific activity ten times higher than the activity of previously described tissues. The rod outer segment also contains phosphodiesterase with a correspondingly elevated specific activity. We have in addition detected a cyclic-AMP dependent protein kinase which phosphorylates histones and rod outer segment membranes. A light inactivated sucrose suspension of rod outer segments recovers half of the initial adenyl cyclase activity after incubation in the dark. Recovery of enzymic activity is prevented by organic mercurials which do not in themselves alter the activity of the light or dark adapted system. Our experiments suggest that cyclic-AMP is an intermediate in the light and dark induced changes in sodium permeability in the photoreceptor cell. The light induced conformational changes in rhodopsin appear to regulate the activity of adenyl cyclase. These findings should permit a molecular explanation of the known physiological characteristics of visual excitation.

INFLUX OF K-42, NA-22 AND CA-45 DURING IN VITRO HORMONE RELEASE FROM THE RAT ADENO-HYPOPHYSIS. J. V. Milligan and Jacob Kraicer. Dept. of Physiology, Queen's University, Kingston, Ontario, Canada.

Hormone release from the rat adenohypophysis, provoked by elevated external [K[†]] is accompanied by an increased influx of Ca-45. When hormone release is provoked by an acid extract of rat hypothalamus-stalk-median eminence (HSME), the Ca-45 influx is not increased. This is not consistent with the "stimulus-secretion coupling" model. Measurement of Na-22 influx and K-42 influx under similar conditions, where hormone release occurred showed that Na-22 influx was unaffected by either procedure. The influx of K-42 was increased in the presence of elevated [K[†]] and was not affected by the addition of HSME. Hormone release provoked by either elevated [K[†]] or HSME will not occur in a calcium-free medium. The influx of K-42 is unaffected by calcium free conditions, but Na-22 influx is increased. Conclusions: Hormone release provoked by HSME is not accompanied by an increased influx of these common cations. Hormone release provoked by elevated K[†] is associated with an increased influx of both Ca^{††} and K[†]. Ca-free conditions may prevent release by allowing an increased influx of Na[†]. (Supported by MRC (Canada), Associated Medical Services, Inc. and Queen's University Loan Fund.)

ANTAGONISM BY NORADRENALINE OF THE CHANGES IN RENAL FUNCTION ASSOCIATED WITH DEVELOPMENT OF RESISTANCE OF THE RENAL VASCULATURE TO THE ARTERIAL INFUSION OF ANGIOTENSIN.

Ivor H. Mills & R. J. Wilson, Dept. of Investigative Medicine, Cambridge, England.

Angiotensin was infused at 0.01, 0.1, 1 or 10 µg min⁻¹ into the left renal arteries of dogs. The lowest dose caused no fall in G.F.R. (C_{IN}). Higher doses caused a fall in C_{IN}, C_{PAH} and excretion of sodium and potassium in the first ten min but no change in urinary osmolality (Uosm). In subsequent ten min periods C_{IN} recovered in all experiments; with 1 µg infusions sodium excretion then rose and Uosm fell on the infused side only. With 10 µg infusions sodium excretion exceeded control levels and Uosm fell on both sides. During the post-infusion periods changes in sodium excretion and Uosm were out of phase. Infusion of noradrenaline into the left renal artery when the renal vessels were registant to angioten sin produced only slight constriction with low doses (1 - 10 µg min⁻¹) but more vasoconstriction when the angiotensin was stopped. Larger doses of noradrenaline (10 - 20 µg) caused a fall in C_{IN} and sodium excretion and a rise in Uosm but they caused complete renal shut down only then the angiotensin was stopped. The data suggest that the resistance of the renal vessels to the vasoaction of angiotensin is associated with a rise in sodium excretion and a fall in Uosm which may be only on the infused side. In appropriate doses these changes are antagonised by noradrenaline. Vascular resistance to noradrenaline is soon lost when angiotensin infusion is stopped.

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SOME PROPERTIES OF THE SLOW WAVES OF THE RABBIT SMALL INTESTINE. R.G. Mills, G.S. Taylor*, M.E. Holman. Dept. Physiology, Monash University, Clayton, Victoria, Australia 3168. (*Research Fellow, Canadian Heart Foundation).

The spontaneous rhythmic fluctuations in the resting membrane potential (often termed "slow waves") have been recorded from longitudinal strips of muscle in a double sucrose gap apparatus and with microelectrodes. Action potentials (AP) were recorded during the peak of slow wave activity in some preparations whilst in others AP's could be induced by means of an increase in (K)₀ or short depolarising current pulses. Using longer pulses (500-900 msec) the frequency of the slow waves could be driven to three times their normal rate. These findings suggest that under normal conditions the coordination of slow wave activity and AP formation can be influenced by electrotonic spread from nearby active regions. Using hyperpolarising current pulses a change in membrane resistance was demonstrated during each slow wave. Depletion of (K)₁ and elevation of (Na)₁ by perfusion with K-free solutions abolished slow wave activity and caused depolarisation. The return of K to such preparations caused an initial hyperpolarisation followed by the return of slow wave activity. However slow waves could not be induced in K-depleted Na-enriched preparations by hyperpolarisation of the membrane potential in the absence of K. These results suggest that the configuration of each slow wave involves a change in membrane conductance and possibly K activated Na pumping.

1169 CORRELATION AMONG DURATION OF MAXIMAL VOLUNTARY APNEAS, BLOOD SATURATION DECREASE AND DURATION OF PHASES OF HEART CYCLE IN MAN. B.D. Milutinović. Dept. of Physiology, Med. Col., Univ. of Novi Sad. Novi Sad, Yugoslavia.

As it was recently presented, heart rate slowed down remarkably in apneas. In all those tests only heart rate and duration of apneas were followed. Still, it is important to know the value of blood saturation, as well as the changes in duration of parts of heart cycle at that time. For that reason sinchronous tracings of polycardiogram, oxyhaemogram and pneumogram were recorded. The tests were carried out on two groups of healthy males, aged 20-22 years. Test-group consisted of 18 well-trained judo experts. As the control untrained subjects a group of medical students /19/was taken. At the rest specific differences in the duration of heart cycle and its various parts between two groups were found. In the conditions of maximal voluntary apneas longer duration of apneas, greater decrease of blood saturation and marked prolongation of the duration of heart cycle and some of its phases in test-group were found. Findings at the rest with significant hypodynamic syndrom in the test-group, as well as the findings at the end of apneas, point at better and more economical heart work, both at the rest and at the end of apneas in this group.

1170 DIRECTIONALLY SELECTIVE UNITS IN THE OPTIC LOBE OF THE FLY AND THEIR CONTRIBUTION TO BIHAVIOUR. K. Mimura. Nagasaki Univ., Faculty of Liberal Arts, Nagasaki, Japan.

A glass microelectrode was inserted into the optic lobes of fleshflies (Boettcherisca peregrina) and discharges responding to the movement of a spot of light were recorded. Directionally selective units were mainly found in the region of the medulla to the lobula, while units, which discharge non-selectively to movement, were found in the medulla only. Furthermore, in the central region from the lobula to the pathways to the central brain were found units of the integrative type, which respond to such complex but continuous movement as a circular motion. That is, analysis of direction is accomplished in the region of the medulla to the lobula, while the integrative action is undertaken by the centrally located units. This tendency is also observed in the speed analysis, because the discharge rate of the directionally selective units in the region of the medulla to the lobula increased proportionally with the logarithm of the speed of the movement, while that in the central region was more complicated. The centrally located units showed integration with other modalities. When air flow was applied to the fly, the discharges in response to the moving spot were either facilitated or inhibited, suggesting the presence of an integrative mechanism between the visual information and the behaviour of flight.

THE STIFFNESS OF PARALLEL ELASTIC ELEMENTS (PE) IN RAT PAPILLARY MUSCLE.

R. Minelli, V. Panagia and C. Reggiani. Inst. of Human Physiology - Univ. of Pavia, PAVIA (ITALY)

Force-velocity relationship of contractile elements in papillary muscle is generally derived from after-load or quick-release contractions. In both cases the influence of PE on the isotonic part of contractions can be minimized but not neglected. Due to stress-relaxation phenomena, the PE's elastic properties cannot be evaluated from load-extension relationship of the whole muscle. After isometric stabilization of the muscle at each different preload level, PE stress-strain relationship have been examined. Quick-releasing the isotonic lever, it could be reduced: 1) the preload on rested muscle, for an extent corresponding to the muscle length variation (diastolic quick-release); 2) both preload and isometric tension during a twitch (systolic quick-release with decreasing passive tension). The results obtained show that: 1) PE stiffness increases with preload level; 2) PE stress-strain relationship is an exponential function; 3) the restitution of parallel elastic energy does not exceed 10% of muscle length. (Supported by italian C.N.R. grant).

ELECTROCHEMICAL DISEQUILIBRIUM FOR H⁺ AND HCO, IONS BETWEEN BLOOD AND CEREBROSPINAL FLUID AFTER 6 HOURS OF VARIOUS ACID-BASE DISTURBANCES WITH AND WITHOUT SUPERIMPOSED HYPOXIA. A.H. Mines, C.G. Morrill and S.C. Sorensen. Dept. of Physiology and Cardiovasc. Res. Inst., University of California, San Francisco, San Francisco, California USA.

Hypotheses attempting to explain the electrochemical disequilibrium ($\Delta\mu$) for H⁺ and HCO₂ between blood and cerebrospinal fluid(csf) have emphasized either (1) active ionic pumps, or (2) passive phenomena, including metabolic production of H⁺ by the brain. Some of the proponents of (1) have proposed that the level of such a pump's activity is altered by changing the arterial HCO₂ concentration or PCO₂, and thus that $\Delta\mu$ should be altered by such changes. Proponents of (2) have argued that only those things which increase the rate of metabolic H⁺ production by the brain, such as hypoxia or extreme hypocapnia, should increase $\Delta\mu$. To gain evidence favoring (1) or (2), we have exposed anesthetized dogs to 6 hours of metabolic acidosis or alkalosis, or respiratory acidosis or alkalosis, or normal acid-base status, both with and without hypoxia. We have measured the acid-base status of cisternal csf and arterial blood during the exposures, calculated the voltage difference between csf and blood from Held, et al., 1964, then calculated $\Delta\mu$ for HCO₃ and H⁺ after 6 hours. The resulting $\Delta\mu$ for HCO₃ in all acid-base states except respiratory alkalosis is about 8.5 mV during normoxia, and about 11.5 mV during hypoxia. This evidence favors (2). Mild respiratory alkalosis (PaCO₂=28 mm Hg) results in a $\Delta\mu$ of about 4 mV in normoxia and about 7 mV in hypoxia. Severe respiratory alkalosis (PaCO₂=15 mm Hg) makes the $\Delta\mu$ about 0 mV in either hypoxia or normoxia. Thus, the data are consistent with (1) in respiratory alkalosis, since the brain's metabolic production of H⁺ should be increased but $\Delta\mu$ is low.

VOLUME, PROTEINS AND CELLS OF PLEURAL LIQUID IN LUNG-CHEST WALL COUPLING. G.Miserocchi and E.Agostoni. Inst. of Human Physiology, Univ. of Ferrara, Ferrara, Italy.

The volume of liquid collected from the costo-diaphragmatic sinus after having opened the chest wall in the head-up posture was 0.46 ml in rabbits and 0.55 ml in dogs; that adherent to the pleural surface was 0.52 and 1.8 ml, respectively. Hence the volume of pleural liquid was 0.98 ml in rabbits and 2.35 ml in dogs. From measurements of pleural surface area and previous data of pleural liquid thickness in the costal regions about 1/2 of the above volume in rabbits and 2/3 in dogs should be located in the marginal and hilar regions. The proteins per 100 ml of liquid collected were 1.33 g in rabbits and 1.06 in dogs. Their colloidosmotic pressure was 4.8 and 3.2 cm H₂O, respectively. The cells per mm³ of liquid collected were 2442±595 (S.E.) in rabbits and 2208±734 in dogs. In rabbits 31.8% were mesothelial cells, 60.8% monocytes, 7.4% lymphocytes, in dogs they were 69.6, 28.2 and 2.2%, respectively. Since the thickness of the pleural space is mostly 5-10 /u, i.e. only a little less than the thickness of these cells, it could be that the contact between the pleural membranes occurs mainly through them.

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THERMOREGULATORY SIGNIFICANCE OF THE EFFECT OF LOCAL SKIN TEMPERATURE ON LOCAL SWEAT RATE. Duncan Mitchell and A.J. van Rensburg. Human Sciences Labs., Chamber of Mines of South Africa, Johannesburg. South Africa.

An acclimatized man rested in dry environments of 35°C, 40° C and 45° C and also worked at 50 W, 75 W and 100 W on a bicycle ergometer at 35°C. During each exposure the temperature of a 10 cm² area of the skin of his forearm was raised to 37.9 ± 0.4°C from 35.3 ± 1.5°C by infrared heating. Sweating from the area was measured using resistance hygrometry. Local sweating varied from 0.2 to 6 g/m² min before local heating. The increase with local heating was directly proportional to the sweat rate prevailing before heating (r = 0.98). This result supports the hypothesis that local temperature affects the efficiency of impulse transfer at the neuroglandular junction. The junction appears to have the properties of a temperature-sensitive amplifier. These properties may also occur at other synapses in thermoregulatory pathways.

THERMAL SENSITIVITY COEFFICIENTS OF DIFFERENT SKIN AREAS. J.W.Mitchell, E.R.Nadel, and J.A.J.Stolwijk. J.B.Pierce Fndn. Lab., and Yale Univ.Sch. of Med., New Haven, Conn., USA.

The current description of thermoregulatory activity has included average skin temperature as a major thermal stimulus, thereby assuming that thermally sensitive elements are uniformly distributed over the skin surface. This proposition was examined by comparing the sweating responses of a reference skin area (thigh) during selective heating of different skin areas. Supine human subjects in constant ambients were exposed to 5-10 minute intervals of constant thermal irradiation. The radiation intensity was either 350 or 700 W/m² and was applied to between 0.03 and 0.10 m² of skin surface. The areas irradiated were the face, segments of the trunk, and segments of the limbs. Internal (esophageal) and non-irradiated skin temperatures remained constant over the 2 hour experiment. The temperature of an irradiated surface increased in proportion to the level of radiant energy and achieved a relative steady state after 3 minutes. A sensitivity coefficient was calculated based upon the thigh sweating rate and temperature and area of the irradiated skin, and for any site was independent of the level of irradiation and size of the area. The relative sensitivity of the facial skin to heating was 3 to 4 times that of the thigh; the chest sensitivity was about 1.5 times that of the thigh, while that for the abdomen and thigh were the same. A comprehensive model accounting for differential sensitivities in the stimulation of the thermoregulatory drive was constructed in accord with these data.

1176 IS THE SACCADIC SUPPRESSION REALLY SACCADIC ? L. Mitrani, St. Mateeff, N. Yakimoff. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Visual thresholds were measured during voluntary saccades of 8° under different conditions. From the experimental data the contributions of the "smearing" and the propre suppression were evaluated. It was found that the suppression disappears when the luminance of the screen is 4.10 nt. On the contrary, the suppression increases when the screen is made uniform by means of black figures on it. Conclusion is made that the "saccadic suppression" is not saccadic but merely depends on the motion of the entire visual pattern on the retina.

A STUDY OF DOSE-DEPENDENCE OF VASOMOTOR REFLEXES ELICITED BY ELECTRIC STIMULATION OF SCIATIC NERVE IN CATS. A.Mitsányi, G.Pavlik, Izabella Morava and A.Erdélyi. Dept.of Experimental Physiology, State Inst.of Occupational Health, Budapest, Hungary. 1177

The magnitude of somatic vasomotor reflexes depends equally on the amplitude and the duration of the stimuli, as well as on the frequency of stimulation and on the duration of the train. An attempt is made to formulate the "dose" of electric stimulation which involves all of these parameters and allows to obtain exact dose-response curves. It is shown that the product of stimulation parameters is proportional - under certain circumstances - to the total energy of stimulation and may be handled as the "dose". The plotting of the pressor responses against the logarithm of this product yields linear relationship, in case the "dose" contains amplitudes and frequencies in the ranges of 8-32 V and of 1-32 cps, reportively (hereat principles of product of the pressor of the product of the pr spectively. Characteristics for short /0.1 ms/ and long /1 and 10 ms/ stimuli are demonstrated in non-anaesthetized, immobilized cats as well as in those anaesthetized with chloralose-urethane. The differences are explained as results of different central mechanisms in the formation of somatic vasomotor reflexes.

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CONTROL MECHANISMS IN RHYTHMS OF PLASMA CORTICOSTERONE. Sherwin Mizell and Daniel P.

Akin. Indiana Univ., Bloomington, Ind. 47401, U.S.A.

Using Rana pipiens the rhythm of plasma corticosterone level has been investigated using a fluorometric method. Animals were maintained under controlled conditions of light and temperature for at least 14 days before sacrifice. Animals were sacrificed in groups of 10-12 every two hours over a 24-hour period and blood obtained by heart puncture. This was repeated at least once a month over a year's time. A seasonal variation in mean (130-156 animals) monthly levels was significant at the 0.001 level. Significant daily rhythms were observed in all months except July, August and early September. The amplitude of these rhythms varied with the time of the year, but all rhythms showed three peaks during a 24-hour period after exposure to a 12:12 LD regime. Adrenal corticosterone content exhibits a significant (0.01) rhythm with a single peak and a period of 22-24 hours. Inverting the light regime led to inversion of the corticosterone rhythm. Experiments with constant light and constant darkness also indicate the lighting regime is important in synchronizing these rhythms. Experiments utilizing blinded and parapinealectomized animals indicate the pineal gland is involved in the synchronization of these rhythms with some modulation through the visual pathways. (Supported by NASA Grant No. 15-003-053.)

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EFFECT OF ISOPROTERENOL, GLUCAGON AND CALCIUM ON MYOCARDIAL OXYGEN CONSUMPTION IN INTACT DOGS. O.D. Migs. Inst. Exper. Med. Res., Univ. of Oslo, Ullevaal Hosp., Oslo, Norway.

The effect of intravenous infusion of isoproterenol, glucagon and calcium on myocardial oxygen consumption (MVO2) has been studied in intact and anesthetized dogs. The dose of each agent was adjusted so as to double maximal rate of rise of left ventricular pressure (dP/dt). Augmentation of MVO₂ was larger (p < 0.025) with isoproterenol (on average 7.9 ml/min·100g) than with glucagon (on average 5.0 ml/min·100g) or calcium (on average 3.4 ml/min·100g). Changes in left ventricular work and left ventricular enddiastolic pressure were similar. Compared with isoproterenol, heart rate increased more (p < 0.001) with glucagon and less (p < 0.01) with calcium. Isoproterenol infusion raised plasma-free fatty acid concentration (FFA) and myocardial uptake of FFA two to three times, but these parameters were essentially unchanged by glucagon or calcium. As mechanical responses to glucagon or calcium were as large as the response to isoproterenol, the additional rise in MVO2 with isoproterenol was probably caused by a metabolic stimulation of high FFA.

1180 COMBINATION RATE OF CO WITH THE ERYTHROCYTE IN THE PULMONARY CAPILLARY.

M. Mochizuki and K. Fukui. Res. Inst. of Applied Electricity, Hokkaido Univ.

Sapporo, Japan.

The overall combination rate of CO with the erythrocyte was calculated in a cylindrical cell model by using the reaction rate of CO with the oxygenated hemoglobin (Fs) and various diffusion rates estimated across the barrier around the erythrocyte. The Fs values used were measured by us at a low PCO range of 3 to 6 mmHg in a highly diluted hemoglobin solution, where it was ascertsined that the rate was independent of COHb saturation, in addition, it was not significantly influenced by diphosphoglycerate and ATP. The calculated overall combination rate was 10 to 20 % smaller than that calculated in a sheet model within a thickness range of the barrier of 2 to 6 μ and no marked reduction of the rate was obtained, even when the thickness was tripled. Since the pulmonary diffusing capacity (D_L) is considered to be an expression of the overall combination rate of CO with a number of erythrocytes flowing through the entire pulmonary capillary for 1 minute, the correlation between the D_L and the above rate was examined by varying the diffusion rate around the erythrocyte. The regression line crossing the origin of the coordinates of the D_L versus the combination rate was obtained, when the barrier thickness was taken to be 2 μ , showing a good coincidence with a morphological figure.

1181 RELATION BETWEEN BLOOD AND LYMPH PROTEINS IN NORMAL AND IN DYSPROTEINEMIC DOGS. Mody E., Szabó S., Reichel C., László I. Departm. of Physiology, Faculty of Medicine, Tîrgu-Mureş, ROMANIA.

Experiments were carried out on normal dogs and on dogs rendered dys-

Experiments were carried out on normal dogs and on dogs rendered dysproteinemic by chronic treatment with colloidal silicic acid. Total protein, glycoprotein and lipoprotein levels and the electrophoretic fractions were determined in blood serum and in thoracic duct lymph before and 30 min after 4 mg/kg histamine injection. In control experoments the alpha_globulin had the lowest, the lipoproteins showed the highest lymph/serum ratio (L/S). After histamine administration there was a five-fold increase of the lymph flow. The L/S of total proteins and of albumin remained unchanged in normal and in dysproteinemic dogs. The L/S of alpha_globulins and -glycoproteins, of beta-globulins and -glycoproteins increased, while L/S of alpha_globulins, gamma-globulins and of alpha_lipoproteins diminished in the normal dogs after histamine administration. The discrepancies between molecular size and L/S ratio of certain protein fractions and the variations of the later values after histamine argue for the existence of a selective filtration of macromolecules through the capillary wall.

SEPTAL-HYPOTHALAMIC INTERACTIONS IN THE CONTROL OF WATER INTAKE. G. J. Mogenson, W. Sibole, J. J. Miller and T. B. Wishart. Departments of Physiology and Psychology, University of Western Ontario, London 72, Ontario, Canada.

Spontaneous water intake in rats was increased significantly by lesions and reduced significantly by electrical stimulation of the septum suggesting that the sental area exerts an inhibitory influence on the lateral hypothalamic "drinking system". To test this hypothesis stimulating electrodes were implanted chronically in the lateral hypothalamus and septum and to ensure that the septal electrodes were correctly positioned electrophysiological recordings were made of evoked responses in the lateral hypothalamus during septal stimulation. After the animals had recovered from the surgery water intake was elicited by electrical stimulation of the lateral hypothalamus using rectangular pulses (duration 0.1 msec, frequency 50 Hz). Pulses of electrical stimulation delivered to the septum 5 msec before each pulse to the hypothalamus increased significantly the frequency of elicited drinking and the volume of water intake. It is concluded that the septum has a facilitatory effect on hypothalamic mechanisms involved in the control of water intake. (Supported by grants from the MRC and the NRC of Canada).

THE DYNAMIC RESISTANCE OF THE CHEST WALL IN THE DOG. P.Mognoni and F.Saibene. Centro Studi Fisiologia Lavoro Muscolare, C.N.R., Milano, Italy.

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The dynamic resistance of the chest wall (R_{CW}) has been measured in 7 dogs anaesthetized and curarized. The animals, in prone position, have been artificially ventilated at different pulmonary volumes, with a pump generating a sinusoidal flow at a frequency of 15, 30, 45 and 60 c/min, with a stroke volume equal to ab. 10% of the individual VC. Flow, volume, tracheal and esophageal pressures have been recorded. At a ventilation corresponding for frequency, depth and lung volume to quiet breathing, the R_{CW} is ab. 50% of the total respiratory resistance of the intubated animals. At increasing flow rates the R_{CW} decreases, indicating that R_{CW} is not a simple viscous resistance; this could be due to plasticity and/or to the different time constants of the structures involved. At a given flow rate, the R_{CW} decreases with lung volume: this could be ascribed to the decrease of tissues linear velocity and/or the chest wall compliance. Lung tissue and chest wall resistance seem determined by different factors.

THE EFFECTS OF NAJA HAJE VENOM AND ITS IONOPHORETIC FRACTIONS ON GLUCOSE METABOLISM. By A. H. Mohamed, M. M. Hanna and R. Selim. Dept. of Physiology, Faculty of Medicine, Ain Shams Univ., Cairo, U.A.R.

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The effects of Naja haje venom and its ionophoretic fractions, in sublethal doses and lethal doses, on blood glucose levels and liver and muscle glycogen were studied in rabbits. The venom caused a hyperglycemic response accompanied by decrease of glycogen concentrations in the liver and muscle. Two different factors were suggested;

- a) In sublethal doses, phospholipase A is the chief factor.
- b) In lethal doses, asphyxia is another possible mechanism. The supposed role of copper ions was considered probable.

ELECTROENCEPHALOGRAPHIC CORRELATES OF INFORMATION PROCESSING IN THE MONKEY (MACACA NEMESTRINA). Samuel L. Moise, Jr. and Anatol Costin. Department of Anatomy, University of California, Los Angeles, USA.

1185

This research is part of a series designed to map the EEG from many brain sites in monkeys during training to perform simple to complex information processing tasks. EEG patterns are assessed by power density spectral analysis, including autospectra, cross spectra, and discriminant functions derived from these variables. Three monkeys were implanted with concentric electrodes in amygdala, hippocampus, hypothalamus, lateral geniculate body, thalamus, septum and optic cortex. These animals were first trained to respond to a white light stimulus, then to discriminate between red and green lights. All training and testing was performed with computer control for presentation of stimuli, selection of parameters, recording, and evaluation of behavioral data (including latencies). The animals were then trained to match to sample where the sample was red, then green, and finally a random selection of red or green each trial. The animals were then trained to match from sample. During training, changes in patterns of EEG in different brain locations were observed. Some of then, particularly in the hippocampus, hypothalamus, and lateral geniculate distinguished stimulus and response parts of trials as well as correct and incorrect performance.

(Supported by USPHS GF02 MH 44,369-01A1 PS and GM 16058-04).

1186 THE FACILITATED DIFFUSION OF CO, IN PHOSPHATE SOLUTIONS. W. Moll. Inst. für Physiologie der Med. Hochschule Hannover, Hannover, BRD.

The steady state flux of CO₂ across 150 μ thick layers of phosphate solutions was measured at 22°C. It was found that after addition of carbonic anhydrase an increase of the CO₂ flux occured, indicating facilitated CO₂ diffusion. The increase was 160°S in a 1/15 m solution (49 mmol/1 Na HPO₄, 17 mmol/1 KH₂PO₄) when the boundary CO₂ partial pressures were 26 and 57 Torr respectively. The rate of facilitated diffusion of CO₂ was related to the carbonic anhydrase concentration up to a concentration of 0.15 g%. In order to obtain additional parameters of the facilitated diffusion of CO₂ the CO₂ dissociation curves of phosphate solutions were determined and used to Calculate the activity coefficients and the concentrations of HCO₂, HPO₄ and H₂PO₄ at different CO₂ partial pressures. From the known electric conductivity and the activity coefficients the diffusion coefficients of the anions were calculated. The maximum facilitated diffusion of CO₂ was proportional to the calculated HCO₃ concentration difference between the two sides of the layer and was related to the ionic strength. The facilitated diffusion of CO₂ was treated theoretically. It could be derived from HCO₃ diffusion coupled with H transport by H₂PO₄ diffusion.

1187 ATPase ACTIVITY IN BRUSH BORDER FRAGMENTS FROM RABBIT KIDNEY CORTEX.

Olaf J. Møller, Inst. of Physiology, Univ. of Aarhus, DK 8000 Aarhus C,

Denmark.

A fraction rich in brush border fragments from cortex of rabbit kidney has a high (Na + K)-dependent ATPase activity. By homogenization the (Na + K)-activity decreased. Treatment of the fraction by deoxycholate restored the activity to the level of the untreated fraction. These results may be explained by assuming that in the brush border fragments the active enzyme sites are accessible for the substrate. By homogenization the fragments are disrupted and the microvilli are transformed to closed vesicles. Thereby the substrate is hindered to reach the enzyme sites. By deoxycholate treatment the vesicles are reopened and the enzyme sites are again available for the substrate and the activity is increased. This interpretation of the deactivation and reactivation is in accordance with and further stresses a model for the activation we have put forward in a previous work. The model implies that the activation of the (Na + K)-ATPase activity by freezing and by treatment with deoxycholate is due to the opening of closed vesicles.

1188 MOTIVATING AND SLEEP-INDUCING EFFECTS ELICITED BY HIGH FREQUENCY STIMULA-TION OF THE SAME MID-BRAIN TEGMENTAL REGION. P.Molnár, L.Lénárd and E. Grastyán. Inst.Physiol.Univ.Med.Sch.Pécs, Hungary.

Two diametrically opposite behavioral and bioelectrical effects, an aversive motivational state and sleep can be elicited with high frequency electrical stimulation of identical parameters of one and the same tegmental locus in different psychological background in chronic implanted cats. In the danger zone of the one-way active avoidance cage, the stimulation consistently activated the previously established avoidance reflex; the same stimulation, however, when administered in the safety zone of the cage, induced an immediate slow-wave sleep. In an indifferent testing cage the tegmental loci able to produce such effects were characterized by ipsiversive circling or withdrawal movements followed by contraversive rebound motor effects. With the "pedal switch-off" technique after several trials, a definite pedal approach reaction developed. On the basis of the present and our earlier findings a critical role of the ipsiversive neural mechanisms in the production of sleeping behavior is proposed.

TRAVAIL DYNAMIQUE LOCAL, POSITIF ET NEGATIF, CHEZ L'HOMME. H. Monod et J. Scherrer. Lab. Physiologie du Travail, CNRS, Paris, FRANCE.

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Une équivalence a été recherchée entre le travail positif et le travail négatif réalisé lors de mouvements alternés de flexion-extension de l'avant-bras sur le bras, mobilisant des charges comprises entre 3 et 9 kg. La fréquence des mouvements a été de 10 et 12/mn, mais la vitesse de chaque contraction était celle adoptée, spontanément, par chacun des 6 sujets étudiés. La séparation du travail positif et du travail négatif ou leur association(qui constitue un travail mixte) ont été faites avec un ergomètre électromagnétique. Trois critères de comparaison ont été retenus : dépense énergétique, électromyogramme et puissance critique (puissance maximale sans fatigue). Des résultats concordants ont été obtenus avec ces trois critères, qui traduisent la mise en jeu de proportions différentes des unités motrices disponibles dans le travail positif et dans le travail négatif, à charge et à vitesse identique : 1) à vitesse spontannée, la dépense énergétique du travail négatif est égale à 1/3 de celle du travail positif; 2) les électromyogrammes intégrés sont dans un rapport identique; 3) la suppression du travail négatif, qui alterne avec le travail positif dans un travail mixte, permet au muscle d'augmenter de 33% sa puissance critique de travail positif.

STATISTICAL NATURE OF PULSATILE BLOOD PRESSURE WAVES STUDIED BY CORRELATION FUNCTIONS IN DOGS: E.Monos, B.Szucs Exper. Res. Dept., Semmelweis Med. Univ. and Dept. of Automat. Technical Univ., Budapest, Hungary.

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In recent years stochastic methods were applied successfully in our dept. for the study of circulatory dynamics. This work raised the question that, how long a period of the pulsatile pressure waves could be regarded to be stationary and that, what kind of signal-components they are composed from. The problem was studied by means of serial autocorrelograms. Pressure signals derived from the ascending aorta and femoral artery were analysed in observation periods of 40 or 200 sec duration by a real-time correlator and were registered simultaneously on a polygraph. It was estimated that pressure waves might be regarded as stationary for periods of about 10 minutes long with a good approximation. Only a slight degree of arythmia is detectable on the autocorrelograms as a well defined stochastic component which was eliminated at a 2 sec delay time. It occured only rarely when stochastic component couldn't be demonstrated on the pressure curves. Velocity of the pressure waves propagation could be determined by crosscorrelograms within a 1 msec. limit.

*B.Szucs, E.Monos: Internat. J. Bio-Med. Comp. 1 (1970) pp 87-102.

SACCADIC INTERACTION ON CELL RESPONSES IN THE LATERAL GENICULATE NUCLEUS. V.M. Montero and L. Robles. Dept. of Physiology and Biophysics, Univ. of Chile, Santiago, Chile.

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The effect of fast phases of vestibular nystagmus on evoked and spontaneous discharges of neurons in the lateral geniculate nucleus of the rat have been studied. In order to determine the central influence of saccadic activity, the receptive fields were stimulated in a fixed eye after sectioning the extraocular muscles. Data analysis was carried out using a LINC computer. Results show that the probability of firing of "concentric" cells decreases from 30-40 msec to 160-200 msec after the onset of saccades, under a wide range of illumination and different visual patterns. The effect was the opposite for "on-off" type of cells, i.e., an increase in discharge frequency occurred with a maximum at about 150 msec after saccades. The time-course of the observed effect allow a correlation to the saccadic slow waves in LGN previously described, and to the psychophysical saccadic suppression phenomenon, if latency of transmission from the retina to LGN is considered. A model explaining a possible mechanism of saccadic interaction in the LGN will be presented.

1192 EFFECTS OF RO 5-4200, A BENZODIAZEPINE DERIVATIVE, ON THE EEG AND THE SLEEP CYCLE IN MAN. J.M.Monti, H.M.Trenchi and F.Morales. Depts.of Pharmacology and Therapeutics and Psychiatry. Hospital de Clinicas. Montevideo, Uruguay.

The action of Ro 5-4200, a benzodiazepine derivative, was studied on the sleep cycle and the EEG of patients with severe insomnia. The compound was administered at the dose of 2-4 mg by oral route, and its action was assessed on some variables of the sleep cycle by means of cortical EEG, EOG and EMG recordings of 8 h duration. Placebo was given during the control period and after RO administration was ended. At the EEG level the compound induced a disappearance of the slow wave activity at all leads, which was substituded by fast waves of moderate amplitude and a significantly higher number of spindles. It was therefore possible to distinguish only 3 states; wakefulness, NREM and REM sleep. The compound produced a consistent decrease of the latency to fall asleep and the number of awakenings. Total sleep time increased at the expenses of NREM and REM sleep. After RO was discontinued there was no rebound of REM sleep. It is concluded that RO 5-4200 is a reliable and effective hypnotic tending to normalize sleep qualitatively and quantitatively.

SODIUM CHLORIDE REFLECTION COEFFICIENT IN RABBIT GALL BLADDER. G. Monticelli, G. Torelli and F. Celentano. Inst. of General Physiology, Inst. of Physics, Univ. of Milan, Milan, Italy.

Membrane selectivity in passive transport is measured by the reflection coefficient $\sigma.$ In actively transporting membranes an apparent reflection coefficient σ_{app} has been introduced. The latter varies with experimental conditions. A relationship between the two coefficients has been derived. Assuming that distinct forces lead active and passive fluxes of the solute, the dissipation function can be written as a function of hydrostatic Δ and osmotic Δ pressure differences and of the "active force" $Y_S.$ From this a phenomenological equation for volumetric flow $J_V=-L_D\Delta\Pi_i+L_Dd\Delta\Pi+L_DaY_S$ is derived, where Lp and L_{Dd} are the hydraulic permeability and ultrafiltration coefficients, L_{Da} a permeability coefficient for active transport and $\Delta\Pi_i=-\Delta_D$ is the osmotic pressure of an impermeant solute. From this equation, introducing $\sigma=-L_{Dd}/L_D$, $\sigma_{app}=\Delta\Pi_i/\Delta\Pi$, $\sigma_a=-L_{Da}/L_D$, when $J_V=0$ the equation $\Delta\Pi_i=\sigma\Delta\Pi-\sigma_aY_S$ is obtained. Preliminary results for NaCl transport in everted rabbit gall bladder show that $\Delta\Pi_i$ values required to zero J_V plotted as a function of $\Delta\Pi$ fit the latter equation.

FIBER OPTIC REFLECTION OXIMETRY. G.A. Mook and M.L.J. Landsman. Lab. of Chemical Physiology, Univ. of Groningen, the Netherlands.

The fiber optic reflection oximeter consists of a fiber optic catheter, containing two bundles of glass fibers of about 150 fibers each, a light source for illuminating the blood via the efferent fiber bundle and a unit for measuring the reflected light transmitted by the afferent bundle. This unit contains a condensor, a dichroic mirror and two filter-photocell combinations, one for measuring the oxygen saturation, the other for compensation of non-specific effects. The photocells are silicium barrier layer cells (Siemens BPY 11). Using integrated circuits the logarithm of the ratio of light intensities at 640 and 920 nm ($\log R^{640}/R^{920}$) is recorded. The instrument has been calibrated by comparing with a Radiometer oxygen saturation meter (OSM 1). Calibration lines obtained with pig blood in vitro are similar to those obtained in vivo in anaesthetized dogs and are almost straight lines. By taking the ratio of light measurements in two spectral regions flow effects are only partly compensated for; the remaining flow artifacts are suppressed by electronic filtering. In a series of 80 in vitro determinations (range 40-100 % sat.) the standard deviation (s) of the differences between the fiber optic oximeter and the OSM 1 is 2.29 % sat. For 53 determinations above 70 % s is 1.62 % sat. Simultaneous records of oxygen saturation and variations of oxygen tension have been made using a platinum tipped fiber optic catheter.

A COMPARATIVE EVALUATION OF SOME PHYSIOLOGICAL NORMS OF SUBJECTS ENGAGED IN DIFFERENT PHYSICAL ACTIVITIES. Sukhendumohan Mookerjee, Dept.of Physiology, Christian Medical College, Ludhiana, Punjab, India.

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616 healthy male subjects in three activity levels were classed in four age-matched groups. Various physiological parameters and some of their responses to standard exercises were studied to note the normal values and compare these norms between active and less active groups, to ascertain the impact of regular physical exercise on the body. The present discussion deals only with metabolism. Under standardized conditions data were collected for basal metabolism, oral temperature, respiratory quotient, blood sugar and cholesterol. The findings were higher BMR, lower oral temperature, raised RQ, elevated sugar and lower cholesterol levels in blood, and inspite of some of these significant differences in the active subjects, the values remained within accepted normal range, rendering valuable indication of the great effect of regular physical activity on body metabolism. This study reveals that certain changes occur in the physiological norms even in basal state, due to regular physical activity and these changes are an attempt of the body to maintain efficiently the homeostatic and homeokinetic mechanism of the individual both at rest and during activity.

5

LASER TEMPERATURE-JUMP TECHNIQUE FOR RELAXATION STUDIES OF THE IONIC CONDUCTANCES IN SINGLE MYELINATED NERVE FIBERS.

L. E. Moore, J. P. Holt, and B. D. Lindley. Dept. of Physiology, Case Western Reserve University, Cleveland, Ohio, U.S.A.

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A temperature jump technique for single nodes of Ranvier has been developed using a high energy pulsed laser system. The temperature perturbation was accomplished by firing the laser beam obtained from a neodymium rod through the solution surrounding a single node. The temperature step was achieved within one msec using the laser in the normal mode of operation. During the voltage clamped steady state current a temperature jump from 4°C increased the current to a new steady state value within the time course of the T-jump. This finding indicates that the maximum potassium permeability, P_{K} , has a rapid relaxation time and that the steady state value of n is relatively independent of temperature. T-jumps applied during the voltage clamped sodium currents showed that the sodium permeability changed with a relaxation time that was also faster than the duration of the normal mode laser output. T-jumps observed during a hyperpolarization or at the resting potential showed no detectable conductance change. When a T-jump immediately preceded a voltage clamp pulse the technique was then used to investigate the effect of changes in the steady state temperature on the ionic conductances. It was found that the magnitude of the change in membrane current due to a T-jump was directly related to the level of cathodal polarization. Supported by USPHS 2ROINBO8409 and NSF GB7668.

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EFFECTS OF AMBIENT AIR AND WATER TEMPERATURES AND DEPTH OF IMMERSION ON APNEIC BRADYCARDIA IN MAN. T.O. Moore, J.A. Setliff, and S.K. Hong, University of Hawaii, Honolulu, Hawaii. Heart rate (HR) responses to 60 second breath-holds (BH) on total lung capacity were recorded during (1) face immersion (FI) in water temperatures of 5°, 15°, 25° and 35°C at ambient room temperatures of 25° and 5°C, (2) ocean SCUBA dives at increments to depths of 60 feet (T° = 26.2° to 26.6°C) and (3) recompression chamber dives at increments to 100 ft in air with face immersions in 25° and 5°C water. During condition (1) maximum bradycardia (25°C room) was 25% and not different in air or 35°C water. In 25° and 15°C water, reduction was 33% and 42% in 5°C water. In 5°C room, maximum reduction was 12-15% less in air and all water temperatures except 5°C, where responses were similar. Hand and finger skin temperatures accounted for most of the variance in the latter data. Under condition (2), reduction during BH at 60, 45, 30 and 15 feet and at the surface was 16%, 19%, 20%, 20% and 27%, respectively. In the chamber dives ((3)) maximum reduction upon FI in 25°C water was significantly greater (29%) at the surface than at any depth (approx. 17%), and FI in 5°C water was 47% at surface vs. approx. 30% at depth. The results indicate that apneic bradycardia is potentiated by FI in cold water; is less during BH in cold ambient air; and that the reflex is attenuated by high pressure with or without whole-body immersion.

1198 AND IN HEALING RICKETS. E. Morava and R. Tarján. Inst. of Nutrition, Budapest Hungary.

The hydroxyproline production /HP/ by metaphyseal bone fragments of normal rats, of rachitic rats, and of rachitic rats supplemented either with vit.D3 or with 25-hydroxycholecalciferol/25-HCC/ was investigated in vitro at 37 C° and at 0 C° respectively. The HP liberation of rachitic bone exceeded that of normal bone. Bones of healing rachitic rats produced more HP to rachitic rat bone. 25-HCC had similar effect to vit.D3, but in case of intravenous administration the lag period of its effect was shorter than that of vit.D3. The HP liberation at 0 C° was about 25% of the HP liberation at 37 C°. If rats fed with a high Ca low P diet were fasted or supplemented with P or deprived of Ca, the inorg.P level of serum increased and the effect of vit.D3 or 25-HCC on HP liberation was stronger. The high HP production of rachitic rat bone seems to reflect a defect of bone collagen metabolism. The further increase following vit.D3 or 25-HCC supplementation thought to be a consequence of the increased turnover of bone collagen. Inorg.P is an important mediator/cofactor in the effect of vit.D on bone HP production.

DIFFERENCES IN THE FUNCTION OF THE NEUROMUSCULAR JUNCTION IN HIBERNATING AND ACTIVE GOLDEN HAMSTERS. J. Moravec, F. Vyskočil, L. Janský. Dept. of Comparative Physiology, Charles University and Inst. of Physiology, Czech. Academy of Sciences, Prague, ČSSR.

In hibernating golden hamsters the activity of the neuromuscular junction in a phosphate buffer (pH 6.5) is maintained in the phrenic-diaphragm preparations at lower temperatures (to 11.3°C) than in active animals (to 16.7°C). At the critical temperature the amplitude of end-plate potentials is decreased, so that it does not reach the critical value for generation of the muscle action potentials. The frequency of miniature end-plate potentials is lower in preparations from hibernating animals (0.07 mepp/sec), than in those from awake animals (0.53 mepp/sec), when measured at the same temperature (20°C); the mean amplitude is unchanged. As is evident from iontophoretic applications of acctylcholine, hibernating animals exhibit greater sensitivity to acetylcholine and the zone of sensitivity to acetylcholine along muscle fibres is enlarged.

1200 INFLUENCE OF THE CORONARY PERFUSION PRESSURE ON THE GEOMETRY AND DISTENSIBILITY OF THE LEFT VENTRICLE. C.Morgenstern, H.Goebel, G.Arnold and W.Lochner, Inst. of Physiology, Univ. Düsseldorf, Germany.

Intracoronary blood volume is enhanced by an increasing coronary perfusion pressure. This change in volume of the ventricular wall reduces the inner diameter of the left ventricle. The outer diameter and the wall thickness increase with elevated coronary perfusion pressure. Time of the experiment, edema of the wall, inflow through Thebesian vessels complicate the measurement of the pressure-volume relation. Excluding these factors the experiments prove, that coronary perfusion pressure is a determinant of the pressure-volume relation of the heart. The coronary perfusion pressure shifts the relation between pressure and volume upwards and to the left.

 $\frac{dp}{dV}$ increases with increasing coronary perfusion pressure, but the elasticity modul $E=\frac{dp}{dV}\times V$ is not changed. These findings will be discussed in relation to the pressure-induced homeometric autoregulation of the heart.

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ACTIVITY OF POSTURAL CONTROL SYSTEM DURING MAINTENANCE OF QUIET STANDING IN MAN. S.Mori. Dept.of Physiology, Hokkaido Univ., Sch.of Med., Sapporo, JAPAN.

1201

The existence of postural control system has been demonstrated in the dog by Brookhart, Mori et al (1965, 1968). The pattern of force exerted on each foot was considered as one of manifestations of the system operation. In order to study the operation of postural control system in man, forces exerted on the feet were recorded during the maintenance of quiet standing posture. Since the ventral surface of foot does not contact with the supporting plane totally, the forces were recorded from fore and hind portions of the foot separately and bilaterally. Patterns of the forces recorded were characterized by an continuous minor alteration and frequency components were quite similar in any portion of foot. Frequency analysis of this alteration shows that the greater part of it is at low frequencies, namely less than 2.0 Hz. With the standing of more than 5 minutes, the higher frequency component which exceeds 10.0 Hz gradually augumented superimposing to the pre-existing slow alteration. EMGs recorded from the gastrocnemius muscle by needle electrode at this occasion exhibited rhythmical burst activities, and they showed a tendency to appear with the above oscillatory phenomenon of the recorded force. Such rhythmical burst activities may be attributable to the impulses circulating the stretch reflex arc. These findings seem to disclose the manner of stretch reflex arc operation during the maintenance of quiet standing posture in man. (Supported partly by the Matsunaga Science Foundation)

PHOTOSENSORY RESPONSES FROM THE PINEAL EYE OF THE LAMPREY (Petromyzon fluviatilis). Y. Morita. Dept. of Physiology, Hiroshima University School of Dentistry, Hiroshima, Japan, and E. Dodt. William G. Kerckhoff-Institut der Max-Planck-Gesellschaft, Bad Nauheim, Germany.

1202

J. Z. Young (J. exp. Biol. $\underline{12}$, 254, 1935) demonstrated in lampreys the effect of removal of the pineal organ on the animals colouration. We investigated the photosensory performance of the pineal organ in situ by recording the action potentials from adult, curarized specimens after removing the lateral eyes as well as from the isolated pineal organ. - From the pineal organ in situ two types of neuronal responses are recorded by means of stainless steel needles: (i) The most common type of neurons is spontaneously active and is inhibited by light pulses above 10^{-5} lm/m² by all wavelengths (λ_{max} 525 nm). During exposure to constant lights of more than 10^{-3} lm/m², the neurons are completely silent except when stimulated by strong light pulses that evoke off-responses (λ_{max} 590 nm). After 5 min exposure to light of 10^8 times threshold dark adaptation is nearly complete after 20 min in darkness. (ii) Occasionally found are neurons excited by light (λ_{max} 535 nm) in the photopic range of luminances. - From the isolated pineal organ slow potentials can be recorded by glass pipette electrodes after dark adaptation with a luminosity function of λ_{max} 525 nm.

1203

MEASUREMENT OF INCREASED VASCULAR PERMEABILITY IN SKIN VESSELS. J.Morley. Division of Immunology, Kennedy Institute of Rheumatology, London, England.

Increased vascular permeability occurring in inflammatory lesions in skin can be measured by the continuous recording of the accumulation of \$^{125}I\$-labelled albumin. A portion of skin (ear tissue in the rabbit, skin fold in the guinea pig) is held in a fixed position relative to a collimated crystal scintillation probe. The animal receives an intravenous injection of ^{125}I -labelled albumin and ^{51}Cr -labelled erythrocytes. Prior to an inflammatory stimulus, both isotopes are intravascular and therefore both count rates represent the blood volume of the area being studied. Following the inflammatory stimulus, the ^{125}I -count rate represents both intravascular and extravascular component. Hence it is possible to record continuously the extravascular accumulation of plasma protein in a skin lesion and so estimate changes in permeability. Use of this method has revealed that the permeability response in cell-mediated immunity is biphasic and that the permeability changes in such lesions in no way resemble those produced by classical antibody.

THE EFFECT OF SHOCK AND RESUSCITATION ON INTERSTITIAL COLLAGEN SODIUM DEPOSITION IN THE PRIMATE LUNG. G.S. Moss, T.K. Das Gupta, and L.M. Nyhus, Dept. of Surgery, The Abraham Lincoln School of Medicine, Univ. of Illinois Col. of Medicine, Chicago, Ill., USA

The object of this study is to describe sodium distribution in primate lung tissue following hemorrhagic shock and resuscitation. Sodium localization methods are based on the electron opaqueness of sodium pyroantimonate. If an unbuffered aqueous solution of pyroantimonate in osmium tetroxide is exposed to lung tissues, then the tissue sodium combines with the pyroantimony to form sodium pyroantimonate. Our method involves the simultaneous perfusion through the pulmonary artery and trachea of an aqueous unbuffered solution of pyroantimonate into one lung of a living baboon. Lung specimens were obtained from control animals, from animals subjected to two hours of profound hemorrhagic shock, and from animals bled and then resuscitated with either isotonic saline or 5% albumin. Control lungs showed random distribution of electron opaque sodium pyroantimonate deposits in the interstitial spaces. In the shock lung, there was a dramatic increase of sodium deposits in the interstitial collagen fibers. In lungs of saline treated baboons, the distribution of sodium pyroantimonate deposits were similar to controls. In contrast, in albumin treated lungs the concentration of electron opaque deposits were essentially state. This data indicates that sodium ions are absorbed in unchanged from the shock pulmonary collagen fibers in substantial quantities during shock. Secondly, saline resuscitation is more effective than colloid in restoring normal pulmonary collagen sodium distribution.

1205 REGULATION OF VENTILATION DURING HYPOTENSION. I. R. Moss and F. F. Kao. Dept. of Physiology, Downstate Medical Center, State University of New York, Brooklyn, NY, U.S.A.

The relationship between various degrees of transient hypotension, produced by peripheral vagal stimulation, and ventilation during hyperoxia, and the effect of such transient hypotension on V-Pco2 response curves during both hyperoxia and hypoxia were studied in 32 nembutal anesthetized and vagotomized dogs before and after carotid sinus nerve section. Ventilation bore an inverse relationship to blood pressure in sinus nerve intact animals, with high ventilation occurring at low blood pressures. After sinus nerve section, the magnitude of the ventilatory increase caused by hypotension was diminished. In sinus nerve intact animals, hypotension shifted the V-Pco2 response curves to the left and upwards during both hyperoxia and hypoxia with an additional increase in slope during hypoxia. After sinus nerve section, hypotension shifted the same curves to the left and upwards only during hyperoxia. From our results we concluded that hypotension caused hyperventilation by both central and peripheral mechanisms. Of the peripheral mechanisms, it was possible to postulate chemosensory mediation between hypotension and hyperventilation. (Supported in part by grants PHS 1-F2-HE 16,302,5T1-CM-968, 5-RO1-HE-04032, NIH, USPHS, Bethesda, Maryland and HRC, NYC, I-194.)

1206 EFFECT OF ACETYLCHOLINE AND NORADRENALINE ON NEURONES IN THE PARAVENTRICULAR NUCLEUS OF THE RABBIT HYPOTHALAMUS. Robert L. Moss, I. Urban and B.A. Cross. Dept. of Anatomy, University of Bristol Medical School, Bristol 8, England.

Responsiveness of individual neurones in the paraventricular (PV) nucleus to microelectrophoretically administered acetylcholine (ACh), noradrenaline (Nor-A), glutamate
and sodium chloride (NaCl)-marking dye mixture was investigated in female rabbits
anaesthetised with urethane. Extracellular recordings were obtained from 110 neurones.
Fifty were identified as neurosecretory by antidromic stimulation of the neural lobe
while the remaining neurones though located in the PV nucleus could not be antidromically
activated. It was thus assumed that these PV neurones do not project their fibers to the
neural lobe. All microelectrode recording sites were determined by microscopic examination of serial sections. The majority of identified PV neurones showed a marked increase in single cell activity during the application of ACh. When tested with Nor-A
these ACh-sensitive neurones displayed a pronounced inhibition. Opposite effects were
observed for the group of PV neurones that were not antidromically identified, i.e. ACh
depression and Nor-A excitation. Glutamate acted as a general excitant to all PV
neurones tested. Equivalent anionic or cationic (NaCl) currents had no influence on
the firing rate of the PV neurones. The results are compatible with a possible functional role for ACh and Nor-A in the paraventricular nucleus of the hypothalamus.

1207

DIRECT METABOLIC ACTION OF SOME BIOGENIC AMINES ON CULTURED NERVOUS TISSUE. R.D.Moucha, V.V.Jinga, I.Mogos, A.Bordeianu. "D.Danielopolu "Inst. of Physiology, Academy of Medical Sciences, Bucharest, Romania."

By continuing studies on the metabolic and morpho-functional characterisation of disperse newborn rat neuroglia cultures in view of establishing characters which are most specific for glial cells, the aspects of the metabolic response of these cells in culture were investigated when adding some neurotransmitter and serotonin to the culture medium. The assays were made from these cultures in the monolayer phase in which the cells exibit a suitable morphologic and enzymatic differentiation, and contact inhibition of multiplication favours the synthesis of RNA which is the specific messenger required for the maintenance of specialized functions. RNA neuroglia cultures varied in terms of the medium content in catecholamines, serotonin or acethylcholine. Accepting the point of view that a RNA transfer takes place between glia and neurons, particularly during intense neuronal activity periods, a direct action of some transmitter on glial RNA synthesis may be significant.

PERFUSED PULMONARY ARTERY WSDGE: DELINEATION OF AN ARTIFACT IN STUDIES ON PULMONARY EMBOLISM. P.V. Moulder, P.O. Daily and E.H. Blackstone. Dept. Surgery, Univ. Pennsylvania and Pennsylvania Hospital, Philadelphia, Pa. USA

n -ced nu-

The perfused pulmonary arterial wedge used previously for studies on pulmonary vasomotion was used to study the reflex effects of large glass bead pulmonary arterial embolization. A modification of the technique in the initial catheter placement was made and when the response to the initial embolization suggested vasodilation, whereas subsequent ones produced no vasoactivity, an artifact was suspected. This was studied by: a) simulating massive embolism by unilateral pulmonary artery occlusion; b) disturbing the catheter in its traversal of the pulmonary artery; c) visual assessment of the surface infusion site during flow and volume changes; d) repetition of small bead embolization studies, performing them with the original as well as the modified method. These studies indicated that the response was an artifact resulting from a change in catheter tip position. After delineation of the artifact the new studies indicate that embolization of the pulmonary arterial bed of the anesthetized dog with thromboemboli or large glass beads (500-840 micra) does not alter the vascular resistance of the perfused pulmonary arterial wedge.

1209

1208

MECHANISMS OF VISUAL ADAPTATION COORDINATION UNDER THE CONDITIONS OF INTENSIVE PHOTOSTIMULATION. A.S.Mozzhukhin, V.I.Shostak. Military Med. Acedemy, Leningrad, USSR.

The process of dark and light adaptation and its mechanisms were investigated after exposure to bright flashes of IOO-2000 mcsec duration, which cause some specific changes in absolute light sensitivity, visual acuity and color and contrast vision recovery as a deviation from Bunsen-Roscow's and Weber-Fechner's laws etc. Under such conditions photochemical processes in retina are characterised by the delay in regeneration of rhodopsin in the initial stage and by the reduction quantum efficiency of flashes down to 0.5. The functional condition of visual system was studied by recording ERG, spontaneous and evoked EEG, estimating eye electrical sensitivity and critical fusion frequency. In these experimental conditions the role of reciprocal inhibition between photopic and scotopic afferent systems proved to be important. The bright flashes cause phase reaction in retina and corresponding nervous centers, that may be interpreted in accordance with linear theory of automatic regulation.

1210 HELATIONS BETWEEN MEMBRANE POTENTIAL AND TRANSITION-VOLTAGE OF RANVIER NODE. H.Müller-Mohnssen and H.Barske. Inst.für Biologie, München, Germany.

In order to examine the influence of some cations on V_m (membrane potential) single Ranvier nodes were circulated by solutions of either NaCl, KCl or CaCl₂. Reduction of [Na'] or [K'] eresp.to c=o (Aqua dest.) causes hyperpolarization; action potentials can be obtained until 1 mM/l[Na'] e, a falling current-voltage, characteristic until 5 mM/l[K']e. Shifts of V_m and V_{Tr} [mV] produced by a tenfold reduction of concentration are observed as follows:

Concentration series	⊿ ^V m	∆ ^V Tr
Ions with high mobility(K'; Na'in presence of veratridine	- 57	-47
Ions with low mobility (Na', Ca'')	-25(59VAP)	-22
K' or (Na') series + 1,8 mM/l Ca''	-59(59VAP)	-12

 V_{Tr} shifts are similar to V_{m} shifts if only one cation species is present. If the solution contains two different cations, Δ/V_{m} and Δ/V_{Tr} diverge. V_{m} is determined by ions with high steady state mobility in the membrane and V_{Tr} by ions which show low mobility but indicate higher interaction with membrane material.

1211 OXYGEN DEPENDENT TRANSPORT MECHANISMS OF RAT JEJUNUM.

B.G.Munck, Inst. of Med. Physiology, Dept. A, Univ. of Copenhagen, Denmark.

Rat jejunum was used in an Ussing apparatus at pH 7.4, 37°C , and with 100% 0_2 . In sugar and amino acid free media the short circuiting current (I_{SC}) is insensitive to N_2 on the mucosal side. N_2 on the serosal side reduces within 5 minutes I_{SC} from about 50 to 15 $\mu\text{amp/cm}^2$. With 28 mM galactose an I_{SC} of 180 - 300 $\mu\text{amp/cm}^2$ is reduced to about 50 by N_2 on the mucosal side and is not significantly reduced by N_2 on the serosal side. In absence of nonelectrolytes I_{SC} is equivalent to the net flux of Cl . With 28 mM galactose the increase in I_{SC} is equivalent to the increase in flux of sodium from the mucosal to the serosal side. The interpretation is that I_{SC} in sugar free medium is caused by a chloride secretion with a cellular location at the base of the villi, and the galactose induced increase in I_{SC} by a sodium absorption located much more apicalli on the villi. The data and their interpretation agree with the sodium gradient hypothesis for nonelectrolyte transport and support the proposal of a secretory mechanism localized in the crypts of Lieberkühn.

THE SUPERIOR COLLICULUS EVOKED RESPONSE AND ITS ENHANCEMENT FOLLOWING PGO WAVES IN THE CAT:
ROLE OF VISUAL CORTEX. J.B. Munson and R.B. Graham. Depts. of Physiology and Psychology,
University of Florida, Gainesville, Florida U.S.A.

Evoked responses in superior colliculus (SC) and visual cortex (VC) produced by electrical stimulation of optic nerve increase in amplitude during the 300 msec following the lateral geniculate spikes (PGO waves) which accompany eye movements of sleeping and awake cats and cats given reserpine (Munson, et al.: Fed Proc 1970). The role of VC in producing SC evoked responses and their PGO-linked enhancement was assessed by stimulating optic chiasm in acute, unanesthetized, reserpine-treated cats and recording potentials bilaterally in SC and VC. SC evoked responses (whether or not they occurred with PGOs) were usually depressed during the cortical inactivation following treatment of VC by KCl or by ethyl chloride or CO2 freeze, indicating that VC tonically enhances SC potentials. In a few less viable animals these procedures depressed only PGO-linked SC potentials, suggesting an additional PGO-linked phasic cortico-tectal contribution. Stimulation of optic radiations produced an SC evoked response which increased in amplitude following PGOs, further indicating a phasic input from VC to SC. Phasic enhancement of SC potentials following PGOs was not entirely of VC origin since it persisted during VC inactivation by KCl depression or freezing. VC apparently contributes both tonically and phasically to the amplitude of SC evoked potentials but is not necessary for their occurrence under these experimental conditions. (Supported by NSF Grant GB 7622 to JBM).

CODING SCHEME IN THE COCHLEA. K. Murata and I. Taniguchi. Div. of Physiology, Inst. for the Deaf, Tokyo Med. & Dental Univ., Tokyo, Japan.

1213

The amplitude of action potential (N_1) in the cochlea is a good measure of the firing probability of neurons responding to click. N_1 's in response to click trains were observed in the cochlea of a guinea pig. Our aim is to analyse the mode of excitability change in the cochlea exerted by irregular nonstationary acoustic stimuli or complex sound as human voice. Based on the double click experiment, responses to any click train with irregular intervals and intensities could be described as follow.

$$E_n = U(I_n) - \frac{n-1}{i} E_i \left\{ 1 - \int \left(\sum_{j=i}^{n-1} T_j \right) \right\}, \quad (n = 2, 3, 4,)$$

E_n: size of N₁ to the n-th click whose intensity is I_n. $U(I_n)$: Intensity-response function to a single click I_n. f(t): recovery process of cochlear excitability after a click stimulus, which is estimated from the experimental data. T_n: interval between n-th and (n + 1)th click.

The first term is the unconditional response to the single click I_n and the second one is the residual sum of suppressions evoked by the preceding clicks. The cochlear responses to the repetitive clicks with constant interval and intensity were well fitted with the above equation. From this result it is revealed that f(t) is fundamental invariant process after a single click in the cochlear excitation and is not modified by any stimulus sequence. On the basis of our analysis the response patterns to a pure tone, AM and FM sound and speech may be well elucidated.

"SOME SUBSTANCES AFFECTING THE DIGESTIBILITY OF CALCIUM AND SECRETION AND REABSORPTION OF ENDOGENOUS CALCIUM IN CONSCIOUS RATS" .- A. Murillo Dept. Animal Physiology .- University of Granade. Spain.

1214

We have studied the effect of some substances that can make calcium to dissolve in the intestinal lumen on the efficiency of its digestive absorption, using diets containing or not sodium oxalate. Oxalate greatly decreased the digestibility coefficient of calcium (D.C.) and this effect was partially compensated by addition of EDTA and sodium citrate to the diet. EDTA had no effect in diets without oxalate but lysine improved the calcium absorption in these conditions. Protein quality clearly affected digestibility of calcium in diets with or without oxalate. Sodium oxalate increased the feacal looses of endogenous calcium. EDTA increased the digestive secretion of endogenous calcium and therefore its fecal excretion. Sodium citrate, sodium lactate, lysine and protein quality also affected the digestive looses of endogenous calcium.

EFFECT OF VARIOUS CATIONS ON THE VENTRICULAR FIBRILLATION THRESHOLD (VFT) AND THE DURATION OF THE INDUCED ARRHYTHMIA. M.F. Murnaghan and M. Ostwald. Department of Physiology, University College, Dublin, Ireland.

1215

Ventricular fibrillation or a rapid tachycardia was induced in isolated guinea-pig hearts (Langendorff preparation) perfused with Locke's solution by applying trains of square-wave pulses of known current strength at set pulse width (0.3, 1, 3 & 10 msec) and length of train (0.2, 0.4, 0.7 & 1.5 sec). Each current strength was tested at a range of frequencies of 20 to 50 cycles per sec to ensure that one of the pulses fell within the vulnerable period of a cardiac cycle. The minimal current strength required (VFT) and the duration of the induced arrhythmia were measured. When guinea-pig hearts were perfused with Locke's solution of normal ionic content the arrhythmia induced was invariably of only a few seconds duration. Low sodium (77 mM) and high calcium (4.3 mM) did not influence the VFT but increased the duration of the arrhythmia induced by the current at all pulse widths and train lengths. Low potassium (1.4 mM) lowered the VFT except with a wide pulse width associated with a long train length and prolonged the duration of the arrhythmia in all tests. Magnesium ions (1 mM) raised the VFT at all train lengths with a long pulse width; it did not influence the duration of the arrhythmia. The results demonstrate that both parameters, the VFT and the duration of the arrhythmia, are of importance in comparing the influence of various agents on induced ventricular fibrillation or tachycardia.

ARTERIAL SMOOTH MUSCLE: TEMPERATURE AND PH DEPENDENCE FOR CONTRACTILE PROTEIN ATPASE ACTIVITY AND SOLUBILITY. R. A. Murphy. Department of Physiology, University of Virginia School of Medicine, Charlottesville, Virginia 22901, U. S. A.

Actomyosin can be extracted from the smooth muscle of hog carotid arteries at low ionic strength. After purification, solubility decreases rapidly with pH and is essentially zero at pH 6 (μ = 0.1). The solubility of the contractile proteins is closely related to ATPase activity and rate of superprecipitation which are optimal at pH 5 - 6 and decrease with a rise in pH. This may explain why thick filaments are rarely observed in situ in smooth muscle unless fixation occurs at low pH (Kelly & Rice, J. Cell Biol. 42:683, 1969). The effects of changes in ionic strength, pH and ATP concentration were combined to isolate arterial actomyosin in high yield, which did not require traces of Ca^++ for ATPase activity and which contained low levels of contaminating myokinase and azide-sensitive ATPases. The temperature dependence of the Mg^++ activated actomyosin ATPase activity (μ = 0.1) in both arterial and skeletal proteins was similar from 20-45 C with an Arrhenius activation energy (Ea) \simeq 14 kcal/mole. At μ = 0.6 with Ca^++ as the activating cation, the enzymatic activity was characteristic of myosin from the dissociated complex. From 15-25 C both arterial and skeletal proteins showed a similar Ea (\simeq 10.5 kcal/mole). However, from 35-45 C the arterial protein Ea \simeq 19 kcal/mole. The myosin-type of arterial ATPase activity greatly exceeds the actomyosin rate and is intermediate between published values for visceral smooth and red striated muscles. (Supported by NIH grant AM-13475.)

1217 COMPARATIVE PHYSIOLOGIC ASPECTS OF HYPOTHERMIA INDUCED BY EXPOSURE TO HELIUM AND COLD. X.J. Musacchia, Gary Anderson, Wynn Volkert and Ramona Chandler. Univ. Missouri, Columbia, Missouri, U.S.A.

Ramona Chandler. Univ. Missouri, Columbia, Missouri, U.S.A.

Hamsters and C3H mice undergo hypothermia when exposed to 80% He+20% O2 (helox) and low temperature, circa 1°C. Hamsters tolerate BT 7°C up to 24 hr. C3H mice are more labile but can tolerate BT 12-15°C up to 9-10 hr and BT 15-17°C up to 20-24 hr. Recovery from helox-cold hypothermia is obtained by exposure to 20-22°C. Hamsters require 1-2 hr to rewarm. Warming curves show two phases, an initial passive warming from BT 7°C to about 15-17°C, followed by an upsurge in slope showing active warming. C3H mice recover in about one hr. Induction requires 4 to 8 hr in hamsters and one hr or less in C3H mice. Hypothermic hamsters are flaccid and limp, whereas C3H mice retain some muscle tone. Cardiovascular and respiratory activity is greatly diminished. In hamsters, EKG's are regular and heart rate 15-18 beats/min. Acute failure is characterized by erratic ventricular beats and depression of the T wave. C3H mice can undergo repeated trials, in contrast, hamsters resist second and third trials by requiring longer induction periods. Cold acclimation (4°C, 2-6 weeks) and hypothermic experiences increase cold tolerance in hamsters. (Supported by NASA Grant 26-004-021 S5 and 6)

1218 RELEASE OF PROTEINS AND ACETYLCHOLINE AT THE NEUROMUSCULAR JUNCTION. J. Musick and J.I. Hubbard. Dept. of Biol. Sciences, Northwestern Univ., Evanston, Ill., U.S.A.

By implementation of a pyrolysis-gas chromatography procedure (Szilagyi, Schmidt and Green, Anal.Chem. 40, 2009, 1968) mixtures of acetyl, butyryl and propionyl choline have been resolved and the pyrolytic derivatives characterized by retention times. Using the isolated rat diaphragm preparation, the quaternary ammonium compounds were precipitated from the tissue effluent after phrenic nerve stimulation. Subsequent chromatographic analysis of the pyrolytic derivatives revealed a single peak with a similar retention time to the pyrolytic derivative of acetylcholine (ACh). The quantity of ACh identified in this way and recovered from tissue effluents was strictly dependent on stimulation parameters. This is taken as evidence that ACh is the only choline ester released at the neuromuscular junction. An independent series of observations on similar effluents using Lowry's protein determination procedure strongly suggest that protein is also released from nerve terminals of the neuromuscular junction in response to nerve stimulation. Characterization techniques including acrylamide gel electrophoresis and electrofocusing suggest that a specific ACh binding protein is released. It is hypothesized that this protein may have functional importance both in transmission and ACh storage.

1219

SEQUENCE OF PATHOPHYSIOLOGICAL REACTIONS OF HAEMOPROTEINS IN THE ANEMIC HYPOXIA. J.Musil. Medical Basic Research, Sandoz Ltd., Basle, Switzerland.

During the inactivation of the oxygen carrying system in the red blood corpuscles a corresponding reaction in the myoglobinsystem of the muscle cell can be observed. This was proved in two series of experiments on white Wistar rats: 1. in an acute reversible methaemoglobinaemia after administration of natrium nitrite, 2. in a subacute methaemoglobinaemia with following partial destruction of haemoglobin after administration of acetylphenylhydrazine. In the first series of experiments 46,6 % of haemoglobin were inactivated 40 minutes after application, whereby in the heart cells were 78,9 % of myoglobin inactivated by forming two physiologically unutilisable components: NO-myoglobin (Fe_2) and metmyoglobin (Fe_3). Determinations were made by using a spectrophotometric three components method. While the part of inactive haemoprotein in the heart cells is greater than in the erythrocytes during the reversible reaction, the destruction of 40 - 50% of haemoglobin was followed by only a slight depression of myoglobin in the heart cells: although myoglobin is very reactive, its steady state and turnover remains stable against a destruction causing influence.

LACK OF EPINEPHRINE INDUCED HYPERGLYCAEMIA IN HYPERSENSITIVE RATS.

L. Muszbek, K. Kovács and B. Csaba. Dept. of Pathophysiology, Univ. Med. Sch., Debrecen, Hungary.

Bordetella Pertussis Vaccine /BPV/ pretreatment increases the sensitivity of rats to shockmediators and anaphylactic shock. As it is known there is a correlation between the anaphylactic sensitivity and the actual blood glucose level in rats.

BPV treatment induced only a moderate decrease in blood glucose concentration, however, the hyperglycemic effect of epinephrine was inhibited. The observed inhibition of the hyperglycemic response showed a good time-correlation with the hypersensitivity caused by BPV. Administration of Prednisolone restored the hyperglycemic effect of epinephrine. Similar observations have been made regarding the cyclic AMP induced hyperglycaemia. On the basis of our results we suggest that the sensitivity increasing effect of BPV is due at least in part to the influence of pertussis on carbohydrate metabolism.

PLASMA VOLUME DURING AND FOLLOWING ACUTE DEHYDRATION BY EXPOSURE TO ENVIRONMENTAL AND WORK STRESSES. Loren G. Myhre and Sid Robinson. Indiana Univ., Bloomington, Indiana 47401, U. S. A.

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Eight unacclimatized young men were rapidly dehydrated by sweating (work in the heat; 4 mets, 50°C db, 26°C wb) and by cold diuresis (rest nude in cold; 18-20°C). Acute dehydration averaging 4.2% of body weight was accompanied by an average plasma volume (PV) decrease of 17% as a result of 2 hours of work in the heat; during 5 hours rest in the cold weight loss averaged 1.4% and was associated with a 15.3% decrease in PV. No significant changes were observed in red cell volume. It was estimated that the PV lost 2.8 and 9.1 times its share of the TBW loss in the heat and in the cold respectively. Following the dehydration exposures, if the men continued in dehydration and rested in a comfortable environment (26°C), within 5 hours the PV had regained averages of 53% and 29% of the losses observed immediately following work in the heat and rest in the cold respectively. The maintenance of water and electrolyte balances during exposures to the same stresses had varying effects: (1) while resting in the cold, water and salt replacement only increased the rate of diuresis with the final plasma loss (16%) being about the same as that observed in the cold without water, and (2) while walking in the heat water and salt replacement reduced but did not eliminate the decrease in PV which averaged 5.6% compared with the 17% decrease observed in dehydration. (Supported by U. S. Army MRDC Contract DA 49-193 MD-2449.)

CONDITIONING AND BRAIN ELECTROPHYSIOLOGICAL AND BIOCHEMICAL CHARACTE-RISTICS IN RATS REARED ON DIFFERENT LEVEL OF ENVIRONMENTAL INFLUENCES. J.Mysliveček, J.Šafanda, Z.Chaloupka, J.Hassmannová. Inst. of Pathophysiology, Charles Univ. Med. Faculty, Plzen, Czechoslovakia.

Rats were reared during the suckling period at different (quantitatively defined) levels of afferent impulses, one group being as control (C) one with increased (I), another with decreased (D) amount of stimuli. Animals were tested at adult age by sets of conditioning (learning and exstinguishing), electrophysiological (evoked potentials to different stimuli) and biochemical estimations (RNA,DNA, phospholipids, ACH-esterase etc). The quality of performance in the higher nervous activity (conditioning) was as follows: I,C,D; in most electrophysiological and biochemical parameters the D group showed significantly impaired values, but differences among I and C group were rather unsignificant. Some electrophysiological and biochemical data of the D group showed similar features as the values detected in rats reared on a low protein diet. Thus two kinds of developmental restriction (sensory and nutritional) showed certain common sequels.

FUNCTIONAL ACTIVITY OF ERYTHROCYTES IN GAS-ENERGY EXCHANGE OF CALVES.

E.A.Nadalyak, L.A.Zabolotnov. All-Union Research Institute of Physiology and Biochemistry of Farm Animals, Borowsk, USSR.

In the experiments on Kholmogor calves at the age 5-120 days it was found that: 1) the erythrocyte diameter in the circuling blood is 3,0-6,7 μ ; 2) with decreasing erythrocyte size their ability to transfer the oxygen also decreases; 3) the erythrocytes with diameter 4,8-5,4 μ have the greatest oxygen capacity; 4) the erythrocyte population with the diameter 4,3 to 6,7 μ actively absorbs oxygen in lungs and gives it up completely to the tissues; 5) with decreasing red blood cell diameter from 4,3 to 3,0 μ their role in 02 transport is sharply deceased and they are taken out from the blood flow; 6) increase of metabolism causes a corresponding increase in erythrocyte functional activity through greater destruction of the cells with diameter 3,0 to 4,3 and increasing the number of red cells with diameter 4,3 to 6,7 μ .

1224 LOCAL AND TOTAL SWEATING DURING EXERCISE TRANSIENTS. E.R.Nadel, J.W.Mitchell, and J.A.J. Stolwijk. J.B.Pierce Fndn. Lab., and Yale Univ.Sch. of Med., New Haven, Conn. USA.

The influences of internal and skin temperatures on the sweating response during the transient phase of exercise have been poorly understood. Three subjects exercised on the bicycle ergometer at 30, 50, and 65 percent of \hat{v}_{02} max in 10, 20, 30, and 40 C ambients for 40 minutes. Continuous measurements were made of major thermoregulatory inputs to the thermoregulatory center: internal temperature in the esophagus and average skin temperature. Total evaporative weight loss and local sweating rate from two skin loci were continuously measured as indices of the thermoregulatory output. Local skin temperatures and $V_{0,2}$ were also continuously monitored. In the presence of ongoing sweating prior to exercise, both local and whole body sweating increased rapidly before any measured body temperature increase occurred. However, in colder ambients and without prior ongoing sweating both sweating parameters tended to follow thermal signals during the transient. The rapid increases in local sweating rate at the onset of exercise were correlated with decreases in R-R interval of the EKG, inferring temporary sympathetic nervous system influence superimposed upon the thermal influences. Total evaporative losses and local sweating rates during the steady state phase were found to be proportional to Tes at constant Ts and proportional to $T_{\rm S}$ at any constant level of $T_{\rm es}$. The local sweating rate was found to be modified also by the local skin temperature. A mathematical model describing these relationships during exercise was able to predict the results obtained at rest.

CORRELATION BETWEEN PERIPHERIAL BLOOD FLOW AND THE LEVEL OF THE SPINAL CORD LESION IN MAN. N.E. Naftchi, E.W. Lowman, H. Sell and H. Rusk. Dept. Pharmacol. and Inst. Rehab. Med.,

NYU Med. Ctr., New York, N.Y. 10016.
Digital blood flow in cc/cm2 skin/min. was measured calorimetrically in the second, fourth, fifth fingers, and the great toes of eight spastic quadriplegic, eight spastic paraplegic and 12 normal subjects. The blood flow in the fourth finger (C7-C8) of quadriplegic subjects (C7-C8) was significantly greater than that in the fifth finger (C8-T1). In normal subjects, the blood flow for these two fingers was the reverse of that in quadriplegic subjects, although in paraplegic subjects (T5-L1) they were almost identical. The second finger (C6-C7) blood flow was almost equal to that of the fourth finger in normal, paraplegic, and quadriplegic subjects. Furthermore, the blood flow in the fourth finger in quadriplegic subjects was significantly higher than that in paraplegic subjects (P<0.05). The blood flow in the fingers of normal subjects was approximately twice that in the great toes. The same was true for quadriplegic patients but it was reversed for paraplegic subjects. The results suggest that paraplegic patients with augmented vasodilation in their lower extremities may compensate for it by vasoconstriction in the upper digital vessels. The finding of increased blood flow in the fourth finger of C6-C8 cord transected patients over that in patients with mid thoracic lesions are in accord with our findings of increased blood flow in denervated organs, supersensitivity to circulating norepinephrine, and greater vasoconstriction in denervated fingers than in the intact ones during hypertensive crisis. Supported by the Edmond A. Guggenheim Clinical Research Endowment.

THE PHYSIOLOGICAL SIGNIFICANCE OF CARNOSINE AGAINST THE INFLAMMATION. Kineshiro Nagai, Dept. of Physiology, Nihon University School of Dentistry, Tokyo, Japan.

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Carnosine in 50mg/Kg ip possesses an anti-edematous action against Carragenin as well as With adenoectomized rats, the anti-edematous action disappears but will be traumatic edemata. restored when Cortisone is conjointly medicated. Conjointly with Cortisone or ACTH, carnosine enhances its anti-edematous action. It promotes the granulations by formalin vitalization. In combination with Cortisone, carnosine further promotes granulations than used alone. action of carnosine which promotes the encapsulation of foreign matters and absorbs edemata is a meaningful expression of the vital defense mechanism. The author advocates a hypothesis that the participation of Cortisone in a vital defense mechanism requires co-factors such as carnosine. On the assumption that all of effective 50mg/Kg ip is absorbed and acts on a localized inflammation without enzymatic changes, an effective amount of carnosine, 50mg/Kg ip, corresponds to 1/40 contained in a vital body. This suggests a physiologic significance of carnosine against the inflammation. Besides, carnosine prohibits an inflammation due to Arthus reaction, serum anaphylactic shock.

ON THE LOCATION OF THE SODIUM TRANSPORT POOL IN THE FROG SKIN. W. Nagel and A. Dörge, Dept. of Physiol., Univ. Munich, Munich, German Fed. Rep.

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In order to receive further information about the nature of the sodium transport pool in the frog skin, the tracer wash out was followed after the skin had been labelled from the epithelial side under different experimental conditions. The wash out of Na-24 to the corium side followed a single exponential function. Approx. 2/3 of the sodium transport pool - as found by tissue analysis - can only be washed out to the corium side (half time 3 min) whereas the remaining part is washed out to the epi-thelial side with a very short half time (less than 30 sec). It must be concluded from these results that the transport pool is divided into at least two parts. The sodium which can be washed out to the corium side seems to be located in a cellular compartment, since the half time of the wash out is increased 3 times after ouabain (10^{-4} M/1). Amiloride appears to block the entrance of sodium into the compartment which can be washed out to the corium side.

(Supported by the Deutsche Forschungsgemeinschaft)

1228 EFFECT OF GLUCOCORTICOID ADMINISTRATION ON LYMPH OXYGEN TENSION IN HEMOR-RHAGIC SHOCK. S. Nagy, T. Barankay, K. Tárnoky, and G. Horpácsy. Inst. of Experimental Surgery, Univ. Med. Sch., Szeged, Hungary.

We have shown earlier that following corticosteroid administration splanchnic (1) and renal (2) blood flows increase in hemorrhagic shock. The question arises whether the increased flow occurred through blood vessels where blood-tissue exchange of oxygen is possible (capillaries), thus affecting oxygen tension of the tissues, or mainly through direct arterio-venous communications. Measurement of lymph oxygen tension provides good information on tissue oxygen tension in shock (3). In the present experiments the thoracic duct was cannulated with a stainless steel tube and lymph oxygen tension was measured continuously by polarography in dogs subjected to hemorrhagic shock. Compared to untreated controls, the group given, during the development of the shock (i.e., not as pretreatment), a single large dose of a potent glucocorticoid type steroid showed a higher lymph pO₂ during oligemia and a longer period of circulatory compensation. Lymph oxygen tension was higher even after reinfusion of the blood. The results suggest that previously reported increases in blood flow in the splanchnic and renal circulations after corticosteroid administration in shock are associated with corresponding oxygen tension changes in these organs. References:

- (1) Nagy, S., Barankay, T., Horpácsy, G., Petri, G.: Europ. surg. Res. 2: 263, 1970.
- (2) Nagy, S., Barankay, T., Horpácsy, G.: Europ. surg. Res., In press, 1970.
- (3) Nagy, S., Barankay, T., Tárnoky, K.: Acta physiol. Acad. Sci. hung. 35: 87, 1969.
- THE EFFECTS OF HAEMORRHAGE ON THE INTRARENAL DISTRIBUTION OF BLOOD FLOW MEASURED BY THE CLEARANCE OF 133 Xe. F.S. Nashat, R.E. Devonshire and J.W. Tappin. Depts. of Physiol. and Physics, Middx. Hosp. Med. Sch., London W.I.

In dogs anaesthetised with pentobarbitone severe haemorrhage of 40–60 ml/kg body weight led to a reduction in the cortical flow from 37l $^{\pm}$ 125 to 146 $^{\pm}$ 70 ml/100 gm/min. Outer medullary flow was reduced from 82 $^{\pm}$ 14 to 44 $^{\pm}$ 11 ml in 45% of the cases; It was increased from 38 $^{\pm}$ 12 ml to 73 $^{\pm}$ 29 ml in 36% of the cases and was unchanged at 42 $^{\pm}$ 4 in the remaining 19%. Of the total Xe injected 89% $^{\pm}$ 6 reached the cortex under normal conditions. This was reduced to 68% $^{\pm}$ 17 in haemorrhage. Reinfusion of blood or the injection of sympatholytic agents returned the picture towards normal. The redistribution described is mainly due to increased sympathetic activity of the afferent arteriole in the cortical nephrons. These findings are compatible with the conclusions of Carriere et al., (Circ. Res. 19, 167–179, 1966) but do not support the assertions of Aukland & Volgast (J. Clin. Invest. 47, 488–501, 1968) that haemorrhage produces parallel changes in the two intrarenal circulations. The discrepancy is methodological. Aukland & Volgast 's method of measuring medullary flow by local electrodes from a small area in the vicinity of the arcuate vessels is invalidated by the presence in this vicinity of blood vessels belonging to cortical nephrons.

1230 HEPATIC ORIGIN OF ANGIOTENSINOGEN. A. Nasjletti and G.M.C. Masson. Research Division, Cleveland Clinic Foundation, Cleveland, Ohio, U.S.A.

From observations in hepatectomized animals, it is generally accepted that angiotensinogen originates in the liver. The validity of this conclusion may be questioned, however, since it can now be assumed that such a procedure causes a release of renin which may contribute to the disappearance of renin substrate. A more direct evidence is presented here by demonstrating that the isolated liver releases substrate. Livers from rats were isolated and perfused at 37°C through the portal vein in a closed circuit which included a pump, a membrane oxygenator and a water manometer. Perfusing fluid consisted of erythrocytes (Ca. 20%) suspended in a solution containing albumin and all nutrients used in tissue cultures. Samples were taken at 0,2,4 and 6 hours and centrifuged. The supernatant was incubated with an excess of rat renin. Amounts of angiotensin formed are directly related to amounts of substrate present. Rates of substrate released expressed in ng/hr/g of liver averaged 15.4 ng in normal rats, 34.2 ng in estrogen-treated rats and 190.8 in 18 hour-nephrectomized rats. The pressor activity resulting from incubation of the perfusate with renin was completely inhibited by anti-angiotensin I. These experiments show that the substrate is released by the liver and that the stimulus due to nephrectomy and estrogens persists in vitro; they do not permit, however, to say whether the perfused liver is still synthesizing or just releasing stored substrate.

STIMULATION OF INTESTINAL ENZYME SECRETION BY CHOLECYSTOKININ-PANCREOZYMIN (CCK-PZ).

E. S. Nasset and J. S. Ju. Children's Hospital Research Laboratory, Oakland, California,
U.S.A.

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The lumen of the proximal 2/3 of rat small intestine was perfused, under urethane anesthesia, with 4.92% galactose solution at 37° - 38°. Perfusate was collected in 15 min. intervals and analyzed for: enterokinase, dipeptidase, alkaline phosphatase, sucrase, protein and DNA. In one set of controls the gut was perfused but no injections were made and in another set 0.7 ml of 154 mM NaCl solution was given i.v. between the third and fourth periods. Without injection enzyme concentrations remained relatively constant for two hours or more but saline injection usually resulted in diminished enzyme concentration. Total protein did not change but DNA increased appreciably after about 1-1/2 - 2 hours perfusion, presumably indicative of accelerated cytolysis of mucosal cells. There was no consistent DNA/enzyme ratio and therefore it seems unlikely that the sole source of luminal enzymes is shed mucosal cells. Since it was possible to increase enzyme concentrations 2 - 6 fold by giving CCK-PZ i.v. we conclude, tentatively, that the response is a secretory phenomenon and not a simple release of enzymes from disrupted mucosal cells. Doses of CCK-PZ at 25, 50, 75 and 100 units/kg were given and the maximal response was obtained with 75 units/kg for all enzymes. Injection of secretin and CCK-PZ evoked the classical response in the pancreas but secretin failed to produce any obvious effect on the intestine. (Supported by USPHS research grant AM-11108. We are indebted to Professors Erik Jorpes and Victor Mutt for gifts of intestinal hormones.)

MODIFICATIONS OF THE RENIN AND ERYTHROPOIETIN OUTPUT IN DECREASED ECV. N.Natcheff, L.Jordanova, A.Logophetov. Dept.of Physiology, Med.Faculty, Sofia, Bulgaria.

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Recent investigations conducted in our laboratory seem to indicate that the control mechanisms of the renin and erythropoietin renal output are based on similar principles. In order to assess the role of the volume stimuli as a regulation factor of the renin and erythropoietin level experiments were carried out on Wistar rats which were subjected to peritoneal dialysis with a 10% glucose solution, adjusted to 5% of the body weight. Thirty minutes following the dialysis, blood samples are taken and the kidneys are homogenized for an estimation of the renin activity. In another group of animals subjected to the same procedure 59Fe is administered 24 hours later for evaluating the erythropoietin activity. The results show that the dialysis provokes both an increase of the renin activity and of 59 Fe uptake which is considered as a more general effect of the induced hypovolemia. It is assumed that the renin and the erythropoietin belong to a common system assuring a normal O2-supply to the tissues.

EFFECT OF COLD STRESS ON BRAIN GAMMA AMINO BUTYRIC ACID. S.Nath, V.V. Subbarao and M.L.Gupta. Department of Physiology, J.L.N. Medical College, Ajmer, India.

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Literature dealing with the changes in the brain GABA during cold stress is negligible, therefore the present communication seeks to discover the effect of acute cold stress on brain gamma amino butyric acid (GABA) content and to correlate the reported changes in the brain excitability on exposure to cold stress. Albino rats were exposed to cold stress of - 20 degrees centigrade for 60 and 90 minutes respectively and the GABA content was extracted chromatographically. Cold stress depleted the brain gamma amino butyric acid content indicating that protein metabolism of brain is altered greatly upon exposure to cold stress.

A STUDY OF CEREBELLAR INFLUENCES ON MONOSYNAPTIC REFLEX RESPONSE. U.Nayar, G.S.Chhina and B.K.Anand. Dept.of Physiology, All India Institute of Med. Sciences, New Delhi-16, India.

Effects of cerebellar stimulation were observed on some of the characteristics of the monosynaptic reflex response (MR), recorded from the nerve to the medial head of the gastrocnemius in the cats, after excluding the ipsilateral gamma loop interactions. Short lasting facilitatory effects were observed on stimulation of a localised area (2.5 x 1.5 mm), predominantly white matter rostro-dorsal to fastigial nucleus and medial to nucleus interpositus. The stimulation of anterior cortical regions, including lobus centralis and culmen, led to prolonged inhibition of the MR. Involvement of brainstem reticular formation areas in these responses and the significance of the effects obtained will be discussed.

1235 THE RMCGRAPHIC CORRELATIONS OF ENDOCRINE DYSFUNCTION IN THE MAMMARY GLAND. C.Neacşu. Institute of Oncology, Bucharest, Romania.

Termographic correspondence was followed up in mastopathy bearing and non-bearing mammary gland as related to the menstrual cycle (7th, 14th, 21st and 28th day). Beside significant thermographic differences (delta T variation between symmetric points of the breasts) related to the days investigated, important variations were also noticed in relation to the concentration of steroid hormones (oestrogens and progesterone). Several groups could be classified as a function of hormonal variation (relative or absolute hyperoestrogeny concerning oestrogen/progesterone ratio). Practic effectiveness of the thermographic examination can be achieved only in relation to the corresponding hormonal investigation.

1236 ELECTRICAL INHIBITION OF UTERINE ACTIVITY IN RAT'S LABOR. C. E. Negreiros de Paiva. Dept. of Physiology & Biophysics, Inst. of Biology, University of Campinas. Campinas, São Paulo - Brazil.

The female rat shows in the last day of its pregnancy, a characteristic pattern of continuously increasing uterine electrical activity, labelling the initiation of labor. It was observed that, during labor, it consists of fusiform trains of 90-120 action potentials, with amplitudes of 1.0-8.0 mv, frequencies of 0.5 to 5.0/sec, lasting 100 to 400 msec. These trains have a mean propagation velocity of 5.0 mm/sec, duration of 30-45 sec, and repeat themselves every 40-60 sec, what leads to the complete evacuation of the uterus. Electrical stimuli (trains of 45-90 d-c pulses, 50 msec duration, intensity 2.0-5.0 v, frequency 1.0-5.0 pulses/sec, with intervals of 35-55 sec), applied to the ovarian ends of the pregnant rat uterus "at term" by implanted bipolar silver electrodes, determined usually the progressive disappearance of the propagated spontaneous activity, and its substitution by the exogenous stimuli artifacts, which were not accompanied or followed by effective myometrial contractions. Consequence of this procedure, expulsion of the fetuses failed to occur, or ceased, if it had already begun.

ELECTRICAL EXCITABILITY OF MOUSE NEUROBLASTOMA CELLS IN VITRO UNDER DIFFERENT CULTURE CONDITIONS. P. G. Nelson, J. Minna, J. Peacock and M. Nirenberg. Nat'l Inst. of Health Bethesda, Maryland U.S.A. 20014.

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Cloned mouse neuroblastoma cells under a variety of culture conditions have been examined for electrical excitability using intracellular microelectrode techniques. In the logarithmic phase of culture growth, cells are small and without processes, resting membrane potentials are low and action potentials cannot be elicited by electrical stimulation. When non-dividing cells are selected by incubation of the cultures in 10^{-5M} aminopterin, these cells*exhibit prominent process development and are capable of generating action potentials. Action potentials also occur in the non-dividing cells of cultures grown in serum free media, but the proportion of cells showing excitability is less in these cultures than in the aminopterin selected cells. When hypoxanthine and thymidine are added to aminopterin treated cultures cell division begins and an increase in the number of cells which do not exhibit action potentials occurs. The expression of the generation of action potentials can thus be altered by a number of culture conditions in a cloned line of neuroblastoma cells.

EFFECT OF MAGNESIUM OROTATE ON THE ENZYME ACTIVITIES OF LYSOSOMES AFTER CHRONIC HEPATIC INJURY. E. Nemesánszky, I. Szelényi. "Semmelweis" Med. Univ. Inst. of Pathophysiology, Budapest, HÜNGARY.

As it was demonstrated in our earlier experiment the activity of some liver enzymes were increased following to a treatment of orotic acid or magnesium orotate.

At the present experiment the activity of two lysosomal enzymes in liver and serum/acid phosphatase and acid ribonuclease/ was examined during liver regeneration. The "total" activities of the "lysosome-rich" fraction were lowered and the "free activities" were elevated by a chronic treatment of carbontetrachloride/CCl./. At the group treated with CCl, and fed a magnesium orotate rich/100/mg/day/ these alterations were less, and the enzyme activities returned to the normal level more rapidly than that of the CCl, control group. The lysosomal enzyme activities in the sera were higher due to the hepatic lesion and the elevations were maximal on the 14th day of the regeneration. The magnesium orotate treatment accelerated the normalization of serum enzymes, too.

According to our results, it seems very probable, the regeneration of lysosomes after cirrhosts induced by CCl₄ were accelerated due to a magnesium orotate treatment.

IURBULENCE IN THE AURTA. R.N. Nerem and J.A. Seed. Physiological Flow Studies Unit, Imperial Col. of Science, London, U.K.

Instanteous velocity waveforms have been measured in the thoracic aorta of the dog, using constant temperature anemometry with a hot-film needle probe calibrated in blood from the animal and inserted by direct vessel-puncture (seed, i.a. & Jood, N.B. 1970. J. Scient. Instrum. 3, 377); the system was capable of following velocity fluctuations to over 500 Hz. In anaesthetised open-chest animals, flow was commonly laminar, with smooth velocity waveforms. High-frequency velocity fluctuations occurred during systole throughout the thoracic aorta following experimental manoeuvres (drug infusions, vagal stimulation) which increased the peak velocity of flow and/or decreased the heart-rate. Spectral analysis of such waveforms revealed appreciable systolic velocity fluctuations at frequencies up to 400 Hz. The difference between normalised spectra for disturbed and undisturbed flows in the same animal, which represents the spectrum of the flow disturbances, lay above about 25Hz and showed a humped distribution; these features sungest the presence of true turbulence. Flow disturbances of this type, which occurred at peak velocities (120-25) cm/sec) and heart-rates (1-4dz) within the range reported for normal conscious animals, were accompanied by systolic murmurs audible at the vessel wall with a stetho-

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EFFECTS OF ACTH ON SPONTANEOUS AND SENSORY EVOKED BACKGROUND (BA) AND UNIT ACTIVITY (UA) 1240 IN HYPOTHALAMUS, RETICULAR FORMATION AND HIPPOCAMPUS OF FREELY BEHAVING RATS. A. Newman Taylor and N. Dafny. Dept. Anatomy, Univ. California, Los Angeles, Calif. 90024, In view of the multiple central actions of ACTH on behavior and neuroendocrine regulation, we studied the effects of ACTH on neuronal activity of components of the limbic system-midbrain circuit in freely behaving rats. Adult male Sprague-Dawley rats (17) were each permanently implanted with microelectrodes (63 μ) in the anterior (AH), lateral (LH) and ventromedial hypothalamus (VMH), mesencephalic reticular formation (RF) and dorsal hippocampus (Hpc). Integrated BA (0.5-10 KHz) was pen-recorded; the potential(s) with the highest signal-noise ratio in each taped record were selected by amplitude discrimination and counted for UA. The predominant effect of ACTH (2.5 or 5 U) on spontaneous BA, monitored for 45 mins post IP injection, was excitation in VMH and Hpc, initial excitation followed by inhibition in AH and no predominant effect on RF and LH. The major effect on spontaneous UA was inhibition at all sites except RF. These differences suggest that ACTH may inhibit cells with large potentials while simultaneously increasing the overall firing rate of certain neuronal pools. BA was enhanced by acoustic stimulation in the untreated rat at all sites except VMH where it was primarily inhibited; ACTH reversed these effects. Sensory evoked UA and ACTH effects thereon ressembled the actions on BA except in VMH which now behaved like the other sites and in RF and LH where responses were biphasic with initial facilitation. These effects of ACTH reflect both direct and steroid-mediated

1241 CERVICAL RENAL AUTOTRANSPLANT IN SHEEP. H. H. Newsome, Medical College of Virginia, Richmond, Virginia, U. S. A.

actions on the central nervous system. (Supported by NIH grant NS 07884.)

Access to the arterial supply, venous effluent, and urinary output of the kidney in conscious animals is available in the present preparation over a period of days or weeks. Autotransplantation of the kidney was done into a cervical skin loop which allows control and monitoring of the renal blood supply, hormonal secretion, and urine output. To date, ten renal clearance studies of five periods each have been done in three sheep to assess kidney function. Measurements include that of urine flow, Na and K excretion, osmolar and free-water clearances, inulin, and para-amino hippurate (PAH) clearances, PAH extraction, and renal venous renin activity. In some studies, comparison was made of the function of the cervical kidney to that of the in situ kidney. Na and K excretion, osmolar clearance, and urinary concentration were similar. Average glomerular filtration rate and plasma flow in cervical kidneys were about half that of in situ kidneys. The PAH extraction, measured only in the cervical kidneys, was somewhat lower than expected. A vascular anastomosis with more efficient flow characteristics is planned for subsequent sheep. The preparation has potential for many uses such as repeated isolated renal perfusion, renal infusion and secretion studies, and sequential evaluation of structure and function.

PURKINJE CELL SPIKE BURSTS IN ELASMOBRANCH CEREBELLUM AS AN INTRINSIC CELLULAR PROPERTY.

C. Nicholson and R. Llinás. Div. Neurobiol., Dept. Physiology & Biophysics, Univ. of Iowa, Iowa City 52240, U.S.A.

Burst responses of Purkinje cells have been regarded as a unique expression of climbing fiber (CF) activation in the frog and cat. It will be shown, however, that in the elasmobranch Purkinje cell the burst response can be produced by depolarization other than that generated by CF activation. Intracellular recordings from Purkinje cells of the cerebellar corpus in thornback ray (Platyrhinoidis triseriata) showed that stimulation of either the cerebellar surface or deep white matter evoked both bursts and single spikes. The EPSP which produced the burst response was revealed by artificial hyperpolarization of the cell and shown to be continuously graded with stimulus strength; thus, the EPSP was generated by the excitation of parallel fiber-Purkinje cell synapses. Prolonged burst responses were also elicited directly by artificially depolarizing the cell with outward current via the recording micropipette. It is concluded that the burst responses directly relate to the intrinsic electrophysiological properties of the neuron (multiple site of spike origin, probably dendritic) and not to the type of input which produces the depolarization. This finding implies that it is not valid to equate bursting in Purkinje cells with CF activation unless an all-or-none EPSP accompanies the burst response. This result also suggests that Purkinje cell bursting may be identical to the bursting properties manifested in other neurons of the central nervous system which lack CF-type afferents.

EFFECTS OF GLUCOSE ANALOGS ON FEEDING AND METABOLISM IN NORMAL RATS AND RATS WITH HYPOTHALAMIC LESIONS. S. Nicolaïdis, A. Epstein, J. Le Magnen. Lab. de Physiologie des Sensibilités Chimiques et Régulations Alimentaires, Collège de France, Paris, France.

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In chronically cannulated rats, intra-cardiac injections of 10 mg 2-d-Deoxyglucose (2DG) rapidly induced consistent eating, whereas another glucose analog, e.g. 3-methylglucose, did not. Hypothalamic hyperphagics responded as well as normal. Hypothalamic sites whose lesions abolished the eating response to 2DG were mapped. Respiratory exchanges under the action of the two glucose analogs were studied and are discussed in relation to their respective effects on food intake.

LACTASE DEFICIENCY AND MALABSORPTION. Nicolaescu T., Stoiculescu P., Bittman E., Schiau S., Stoenescu R. "D.Danielopolu" Institute of Normal and Pathological Physiology, Bucharest, Romania.

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A fall in jejunal lactase under the normal values (1 µ/g of intestinal mucosa-Dahlqvist method), affects lactose absorption causing clinical disorders and a flattening of the hyperglycemia curve following ingestion of the disaccharide. Lactase deficiency was investigated indirectly in 63 subjects with milk intolerance selected from 137 with complaints of irritable colon. The clinical test of lactose intolerance (50 g substance in 300 ml water was positive (abdominal cramps and diarrhea) in 47 and the biochemical test too (glycemia curve during 2 hours, without rising by more than 0.20 g/%0) in 45 patients. This positivity was considered the chief argument for chronic dysenzymatic enteropathy due to lactase deficiency in 44 cases. The clinical and biochemical tests were confirmed radiologically, thus emphasizing lactose intolerance (hyperkinesia and dystonia of the jejuno-ileum after ingestion of a 50 g lactose + 300 ml barite mixture). Intestinal lactase deficiency determined genetically and/or ecologically induces lactose malabsorption and accounts for 32 per cent of the cases of clinical irritable colon-like disorders (intermittent diarrhoea).

VENTILATORY RESPONSE TO ALTERED VENOUS CARBON DIOXIDE LOADS IN GALLUS DOMESTICUS. T.E. Nightingale and M.R. Fedde. Dept. of Physiological Sciences, Kansas State Univ., Manhattan, Kans. 66502, USA.

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The control of respiration was studied in anesthetized, spontaneously breathing, adult, Single Comb White Leghorn chickens by intravenous infusion of blood (30 sec at 38 ml/min) containing low, normal, and high CO₂ concentrations into the right atrium. End-expiratory PCO₂, tidal volume, and vertical sternal movement decreased within 4.0 sec after the start of infusion of low CO₂ blood and increased within 4.7 sec after the start of infusion of high CO₂ blood while remaining unchanged during the infusion of normal CO₂ blood. Arterial blood pressure, heart rate, and respiratory rate were not significantly altered by any infusion. The chicken was able to adjust its ventilation to the imposed CO₂ loads so that PaCO₂ remained unaltered. Tidal volume was a linear and reproducible function of end-expiratory PCO₂ and was not related to PaCO₂. The results suggest that the intrapulmonary CO₂-sensitive receptors may serve as primary detectors in the control of tidal volume during normal breathing.

(Supported by NSF Grant GB-3594 and by the KSU Agricultural Experiment Station.)

- 1246 DYNAMIC SENSITIVE-MOTOR PROJECTION. A.Nigro. Lab.of Psychology, Magistero Messina University, Messina, Italy.
 - 1. The dynamic sensitive-motor projection covers the cortical area in a direct relation, in the considered moment, to the function in action. We can thus believe that this area expands and contracts in relation to the intensity of the same action. 2. The dynamic projection takes place when there is an intention of the action or of the sensation, that is, in the circumstances in which the attention intervenes. 3. The presence of an operative pattern, that foresees the use of a particular district of the organism, determines in the cortical zone an area of excitement more extensive than static projection connected with sensitive-motor function of that district. The stimulation of a part of this zone of projection cannot be but related to the function of interested district in the aforementioned operative pattern. 4. An experimental demonstrative system is arranged.

THE EFFECT OF SYMPATHETIC EFFERENT DISCHARGE ON THE ACTIVITY OF ARTERIAL MECHANORECEPTORS IN THE KIDNEY IN THE RABBIT. A. Niijima. Department of Physiology, Niigata University School of Medicine, Niigata, Japan.

The effects of sympathetic efferent flow in renal nerves on afferent discharges from renal arterial mechanoreceptors were observed in dissected filaments of renal nerves. An increase in afferent discharge rate was observed during and after renal nerve stimulation in excised kidney preparations. In vivo, modification of blood pressure levels by chemical and mechanical means, applied during clamping of abdominal acrta above the renal arteries, modified renal afferent discharge rate.

It is suggested that there is an efferent control mechanism on the activity of renal arterial mechanoreceptors by a vasomotor reflex.

THE EFFECT OF CONTINUOUS LIGHT ON PINEAL METABOLISM. I. Nir. Dept. of Applied Pharmacology, Sch. of Pharmacy, Hebrew Univ., Jerusalem, Israel.

Exposure of female rats to continuous light from the day of weaning - 21st day of age - for ten, twenty and thirty days caused a significant inhibition in their pineal RNA and protein synthesis, amounting to 20 per cent when compared with control animals kept in alternating light and darkness. The main inhibition occurred within the first ten days of exposure, coinciding with the period of most active physiological production of nucleotides and proteins. A significant increase in the pineal lactic acid occurred simultaneously under continuous light, but only after twenty and thirty days' exposure. The high lactic acid levels indicate suppressed oxidative cell processes, evidently a consequence of the previously depressed protein metabolism. No change was found in the pineal DNA levels of rats exposed to continuous light, suggesting that the gland's reduced RNA and protein contents result from decreased cellular metabolism and are not related to physiological cell multiplication. This would imply an inhibition of parenchymal hypertrophy of the pineal under continuous light. The concentrations of nucleic acids, protein and lactic acid in the pineals of rats kept in continuous darkness did not differ from those of the control animals.

ELECTROPHYSIOLOGICAL AND ANATOMICAL PROPERTIES OF MAMMALIAN PARA-SYMPATHETIC GANGLION CELLS. S. Nishi and D. D. Christ. Neurophysiology Lab. Dept. of Pharmacology, Loyola Univ. Med. Ctr., Maywood, Illinois, U.S.A.

1249

Ciliary ganglion cells of the cat were studied with intracellular recording and staining techniques. Following recording various membrane potentials, a fluorescent dye (procion yellow M-4RS) was injected iontophoretically into the cytoplasm through the recording electrode: The dye stained consistently the soma, dendrites and axon. Correlation of electrotonic potentials of each neuron with its geometrical dimensions revealed that the dendrites contributed more than 80 % of the total membrane conductance and that the membrane resistance and capacitance for a unit area were approximately $10~\text{k}\Omega\text{cm}^2$ and $1~\text{\mu}\text{F/cm}^2$, respectively. Analysis of spike components in antidromic, orthodromic and direct responses indicated that the membrane of axonhillock area had a lower threshold than the soma-dendritic membrane. The majority of neurons were of B type. Most cells were innervated by two or more presynaptic fibers, but B and C fibers exclusively innervated B and C cells respectively. (Supported by NSF Grant GB-8718 and NIH Grant NSO6672).

THE FIRST AND SECOND SOMATOSENSORY AREAS COMPARED WITH REGARD TO A TACTILE CONDITIONED REFLEX. U. Norrsell. Dept. of Physiology, University of Göteborg, Göteborg, Sweden.

1250

Dogs have been trained to react by an instrumental conditioned reflex to light tactile stimuli. Unilateral ablations of the first and second somatosensory areas have been found to cause a reproducible temporary reduction in the ability to elicit the reflexes from the peripheral fields corresponding to the areas removed. This finding indicates that elements located in these areas normally participate in, or control such reflexes (Norrsell, U., Physiol. Behav. 1967. 2. 73-81). In an attempt to judge whether one or both areas participate, a comparison has now been made between the effects on such reflexes of removing the first or second somatosensory area unilaterally; alternatively bilaterally in one operation. In contrast to the effect of removing the two areas simultaneously, these lesions can be made without causing any deterioration of the reflex. It thus appears as if the suggested dependence of the reflex on the cortical somatosensory areas could be attributed to either area, possibly equally to both.

PROPERTIES OF NEURO-ENDOCRINE CELLS ANTI-DROMICALLY ACTIVATED BY PITUITARY STIMULATION IN THE UNANESTHETIZED RABBIT. <u>Donald Novin</u> and <u>Ross Durham</u>, Dept. of Psychology, Univ. of California, Los Angeles, USA.

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Cells in the paraventricular (PV) and supra-optic (SO) nucleus were anti-dromically activated using a stimulating electrode placed in the pituitary gland. After all surgery was completed the rabbit was taken off general anesthesia (Halothane) and was then held rigidly but painlessly by a bolt cemented to the skull while kept in same planes as in the stereotaxic instrument. Local anesthesia, flaxedil and artificial respiration were then used to maintain the animal. Spike shapes and latencies were similar to those observed in the anesthetized preparation. Spontaneous activity was elevated over what was observed under anesthesia especially in SO. Furthermore, a majority of these cells showed activity closely correlated with the spontaneous change in the cortical EEG from wakefulness to deep sleep. The effects of stimulation of amygdala and hippocampus on SO and PV unit activity were largely explicable by observation of the effects of this stimulation on the EEG. Thus, a typical SO cell had a faster rate of activity in deep sleep than in the waking state. If limbic stimulation desynchronized the cortical EEG it would inhibit the cell. This relation between EEG and unit activity may account for the diurnal pattern seen in the hormonal output of the posterior pituitary.

DISTRIBUTION AND MOVEMENTS OF SODIUM IN FROG VENTRICLES PERFUSED WITH NORMAL AND SODIUM-FREE RINGER SOLUTION. I. Novotný and C. P. Bianchi. Dept. of Pharmacology, Univ. of Pennsylvania, Philadelphia, USA and Inst. of Zoology, Charles Univ., Prague, Czechoslovakia.

Fast rate of sodium exchange across the cell membrane together with high concentration of sodium in the extracellular fluid affects unfavourably the estimation of sodium distribution and sodium fluxes in the heart ventricles. To overcome these difficulties we employed as a washout fluid Ringer solution in which NaCl was replaced by choline chloride. On the basis of the washout curves the resting sodium influx and sodium influx per beat were estimated as 2 pmol/cm²/sec and 8 pmol/cm²/beat, respectively.Rate coefficients of the loss of radioactive sodium indicate that the loss of radioactive sodium was slowed down in choline Ringer solution. This appears to be caused by calcium. The washout studies also revealed that the intracellular sodium content is low (4 mM/kg) and that besides sodium present in extracellular fluid there is a sodium component contained in an unidentified extramyocellular space (12 mM/kg). This component was found only in winter season.

ACTION OF ALDOSTERONE, GROWTH HORMONE AND THE SPIROLACTONE SC 14266 ON THE SHORT-CIRCUIT CURRENT ACROSS ISOLATED FROGSKIN. D. M. Nutbourne, J. D. Howes and N. E. Ferguson. Dept. of Med., Fulham Hosp., London, W. 6., England.

Isolated living skins were obtained from 2 groups of frogs. Group A frogs were kept at room temperature and Group B at 4 C. The addition of aldosterone to the fluid bathing the skin, had no effect on the short-circuit current across skins from Group A frogs; aldosterone caused moulting of the outer layer of the skin when Group B frogs were used. Growth hormone had no effect in the skins of either Group and did not modify the action of aldosterone. A few skins from Group B frogs moulted spontaneously in the absence of aldosterone, After this moult, aldosterone-caused a delayed rise in short-circuit current; this rise was ablished by the spirolactone SC 14266 (2 x 10 M) indicating that the spirolactone was acting as an aldosterone antagonist. However, higher concentrations of SC 14266 (7 x 10 M to 7 x 10 M) (in the absence of aldosterone) always caused an immediate and reversible fall in the current across skins from both Groups of frogs. As aldosterone did not cause a rise in sodium transport in these skins, we therefore conclude that the spirolactone also had a direct action on sodium transport in frogskin which was not due to aldosterone antagonism.

CORRELATION OF HIPPOCAMPAL THETA ACTIVITY TO PASSIVE AVOIDANCE BEHAVIOUR AND PITUITARY-ADRENAL FUNCTION IN THE RATS. Cs.NYakas and E. Endrőczi Research Division, Postgraduate Medical School, Budapest, Hungary.

Recording of hippocampal electrical activity was performed during exploration, in conditioned fear situation and during development of passive avoidance response in a conflict situation of thirst versus fear in adult male rats. Appearance of hippocampal theta activity was closely correlated to the intensity of exploratory activity, and showed an inverse correlation to the pituitary-adrenal response. Duration of hippocampal theta activity showed a close correlation to the duration of intertrial intervals of passive avoidance learning which had been dissociated after corticosteroid administration. It was found that appearance of hippocampal theta rhythm cannot be regarded as electrical correlate of the motivational state per se, and its presence is more related to an expectancy state to integrate a goal-directed motor response. Corticosteroid administration results in a suppression of both integration of goal-directed motor reactions and appearance of hippocampal theta rhythm in motivated situations.

THE HEMODYNAMIC AND METABOLIC EFFECT OF 2,4 DINITROPHENOL AND DIBENZYLINE ON DOGS. I.Nyáry, E.Dóra, K.Ikrényi, A.G.B.Kovách. Exper.Res.Dept., Semmelweis Med.Univ., Budapest, Hungary.

1255

According to Kovách et al. the O2 consumption of mitochondria measured with or without DNP was strongly reduced by Dibenzyline. In the present paper this kind of antagonistic effect of DNP and Dibenzyline was studied under i n v i v o conditions on dogs. Hemodynamic analysis was accomplished, O2 consumption as well as CO2 production were recorded and the arterial blood concentration of glucose, pyruvate and P2 was determined. After administration of a single dose of 4 mg/kg DNP no changes in cardiac output and blood pressure were observed. On the other hand the heart rate as well as the rate of O2 consumption and the concentration of pytuvate and P1 in blood increased. In Dibenzyline pretreated animals /5 mg/kg administered 24 hours before the experiments/ the effect of DNP was considerably diminished.

⁺A.G.B.Kovách, E.Koltay, E.Kovách, Fourth International Congress on Pharmacology, July 14-18 1969, Basel 1969, 140 p. Abstracts.

INFLUENCE OF PLASMA HYPEROSMOLALITY ON BLOOD VISCOSITY IN VITRO AND IN AN ISOLATED VASCULAR BED. S. Nybo Rasmussen. Inst. of Medical Physiology B, University of Copenhagen, Denmark.

1256

Altered viscosity of blood with increasing osmolality have been demonstrated in vitro after addition of nonpermeant solutes, e.g. NaCl (Schmid-Schönbein and Wells, Pflügers Arch. 1969. 307, 59-69, and others). The present study was undertaken to examine the effects of plasma hyperosmolality on blood viscosity in an isolated vascular bed (rabbit ear) as well as in vitro (cone-plate viscometer). Hyperosmolality of ox-blood (up to 950 mosm/kg) was produced by adding NaCl. The rabbit ear was perfused at constant pressures with red cell suspensions as well as with the pure suspension media. The apparent viscosity of a red cell suspension relative to the suspension medium was calculated from the corresponding flow ratios. Both the relative viscosities measured in vitro and in the vascular bed were increasing with increasing osmolality, the maximal increments amounting to about 100%. This phenomenon must be attributed to the red cells and may have important consequences in the renal medullary circulation; it may at least in part explain the inverse relationship between renal medullary blood flow and the medullary hyperosmolality demonstrated by Thurau et al. (Pflügers Arch. 1960. 270, 270-285).

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ON THE ROLE OF THE FRONTAL CORTEX IN THE VEGETATIVE BEHAVIOUR. F.Obál, M.Sz.Vicsay, Gy.Benedek, J.Szabó. Inst.of Physiology, Univ.Med.Sch.Szeged, Hungary.

In rats, conditioned reflex was developed as a result of a decrease in body temperature and O2-consumption, induced by hypoxia; inhalation of an air of 8 to 10 per cent O2-content. The conditioned answer manifests itself in the increase of temperature and O2-consumption. After the extirpation of frontal cortex, the decrease of the effect of hypoxia is unchanged during the associations, but the conditioned answer in the opposite direction cannot be elicited. There develops a quick habituation to histamine /40 mg/kg/injected two to three hours, i.e. after the third or fourth injection, the body temperature does not decrease any more. This habituation ceases to be immediate if, for eliciting the conditioned answer, distilled water is injected into the rats instead of histamine. After the frontal cortex being extirpated, the quick habituation to histamine develops as before, but the injection of distilled water does not elicit any dehabituation. A more extensive extirpation of other cortical areas does not have a similar effect.

1258 CIRCULATORY RESPONSES TO ELECTRICAL STIMULATION OF MEDULLATED AND NON-MEDULLATED AFFERENTS IN THE CARDIAC NERVES. B. Öberg and P. Thorén, Univ. of Göteborg, Sweden.

Heart receptors signal through both medullated and non-medullated fibres. These two fibre groups are reasonably connected to different types of receptors with regard to their localization and function. - In the present study circulatory responses to electrical stimulation of the medullated and non-medullated fibre groups were analyzed in chloralose-anesthetized cats. The right cardiac nerve was freed for about 1.5 cm, cut and stimulated distally while the evoked compound potential was recorded as far proximally as possible along the nerve. Low intensity, high frequency afferent stimulation (4 V, 0.02 msec, 30-60 imp/sec), activating only a group of large fibres (conduction velocities 10-25 m/sec), produced only minor reflex circulatory responses consisting of a moderate increase of blood pressure and heart rate. Higher intensities (4 V, 1 msec), engaging also thin, non-myelinated fibres (conduction velocities 0.5-1.2 m/sec), produced a marked blood pressure fall and a substantial bradycardia with stimulation frequencies as low as 4-5 imp/sec. The results suggest that the main reflex influence of cardiac receptors on the circulatory system is exercised by receptors signalling in thin, unmyelinated fibres, while receptors firing in thick medullated fibres, as e.g. atrial receptors, have a minor immediate influence on the cardiovascular system and then rather of an excitatory nature (c.f. Ledsome and Linden 1967). Reference: F.R. Ledsome and R.J. Linden, J. Physiol. 1967. 193. 121-129.

SODIUM-SENSITIVE COMPONENT OF CONTRACTION ACTIVATION IN MAMMALIAN MYOCARDIUM. R. Ochi and K. Kohama. Dept. of Physiology, Faculty of Med., Univ. of Tokyo, Japan.

The influence of external Na on cardiac contraction was studied in Guinea-Pig's papillary muscle. Membrane potential was controlled by a voltage clamp technique utilizing a sucrose gap and microelectrodes. A constant depolarization could be applied in spite of the change in ionic composition and accompanying contraction and membrane current were simultaneously measured. The preparations were stimulated usually repetitively by clamp pulses at a rate of 0.5-1/sec. When bathing fluid was changed from Na Tyrode solution to cholin- or Tris solution, contraction was increased in about 30 sec. Remarkable increase was observed only in the rising phase or twitch-like component of contraction. The early phase of contraction had been concerned with staircase in Tyrode solution. The succeeding component of contraction was rather insensitive to external Na but was depressed in Ca-free solution. A similar increase of the early phase of contraction was appreciated already at the first contraction in Na-free solution if pulse interval was prolonged to 30-60 sec. Slow inward current carried by Na and Ca ions was decreased in low Na solution. However, it was difficult to evaluate Ca current precisely. The present increase of sodium-sensitive component of contraction can be tentatively explained by assuming that a given depolarization releases more Ca from Na-Ca competitive membrane to myofilament in low Na solution.

LOCAL SUPPLY OF ENERGY TO THE FAST AXOPLASMIC TRANSPORT MECHANISM IN MAMMALIAN NERVE FIBERS

Sidney Ochs. Dept. of Physiol., Indiana Univ. Med. Cent., Indianapolis, Ind., U.S.A.

The transport of materials in mammalian nerve fibers from their site of synthesis in the cell bodies, was studied by injecting cat lumbar 7 dorsal root ganglia with ³H-leucine and at later times removing and sectioning the sciatic nerves to determine the distribution of activity. A crest of labelled materials was found, moving at a rate close to 400 mm/day. Transport at the same rate and with the same crest shape was found to occur when the nerves containing incorporated materials were placed in chambers filled with 95% 0₂ + 5% Co₂ at 38°C. Using this in vitro system, fast transport was blocked within 15 min with N₂ asphyxiation or with NaCN, azide or DNP present. The hypothesis advanced is that ATP produced by oxidative metabolism supplies energy to the mechanism responsible for transport - "transport filaments", sliding by means of ATP-activated cross-bridges along the stationary elements; the microtubules and/or neurofilaments. Particulates, soluble proteins, and polypeptides bound to the "transport filaments" are thus carried down the fiber. The relation of the supply of ATP to the transport mechanism was studied by covering a short stretch of the nerve with petrolatum so that 0₂ could not diffuse through it. Such local anoxic regions placed in the advancing path of fast transport produced a block, with damming of labelled material just above the anoxic region and no penetration of activity into it. The results show that the mechanism of fast transport is present all along the entire length of the nerve fiber. Supported by PHS No. 08706, NSF No. 7234, and the Hartford foundation.

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COMPARISON OF UREA EXCRETION PRODUCED BY INGESTION OF UREA AND OF MEAT. W.J. O'Connor and R.A. Summerill. Department of Physiology, University of Leeds, Leeds, England.

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In these experiments dogs in a normal state of hydration with urine flows of 0·1 - 0·2 ml/min were given a single dose of 10 or 30 gm/kg of lean raw meat. Plasma urea concentration increased to a peak after 6 hrs or more depending on the dose. The urinary excretion of urea increased more than in direct proportion to the plasma concentration; the exogenous creatinine clearance increased by 40 - 50%. The urine volume increased by only 0·1 - 0·2 ml/min with urinary urea concentration of 1,300 - 1,500 mM/l. Doses of urea were given by stomach tube sufficient to produce equal increases in plasma urea concentration; urea excretion was less than after meat and was approximately proportional to the increased plasma urea concentration. There was little, if any, increase in exogenous creatinine clearance. Urine volume was unchanged, with urine urea concentration sometimes exceeding 2,000 mM/l. It would thus seem that the apparent increase in G.F.R. produced by meat cannot be accounted for by the increased plasma urea concentration.

CONDITIONS REGULATING AMMONIA PRODUCTION FROM GLUTAMINE IN THE KIDNEYS OF NORMAL AND ACIDOTIC DOGS. D.J. O'Donovan and R.F. Pitts, Cornell University Medical College, New York, N.Y., U.S.A.

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The factors affecting the activity of renal glutaminase of the dog were determined. The importance of transport across the cell membrane and the mitochondrial membrane were evaluated by assaying the enzyme activity of the kidney slice, homogenate and sonicated homogenate. The activity of glutaminase was increased not only by phosphate but also by many organic acids. Sonication of the homogenate did not alter the glutaminase activity in the presence or absence of these activating compounds. However the glutaminase activity of the homogenate was higher than that of the slice. This indicates that transport of the substrate and/or the activator across the cell membrane limits the activity of glutaminase in vivo. In contrast to the rat acidosis did not alter glutaminase activity or the activation of the enzyme by phosphate or organic acids. It is concluded that the concentrations of activating compounds rather than the amount of enzyme per se may be important for regulating ammonia production from glutamine by the dog kidney in acidosis.

GUSTATORY IMPULSE DISCHARGES IN CHORDA TYMPANI FIBERS OF MACAQUE MONKEYS.
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Univ. Med. Sch., Kumamoto, Japan.

Dept. of Physiol., Kumamoto

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Chorda tympani fibers in macaque monkeys responded to various artificial sweet substances such as saccharin sodium, dulcin and sodium cyclamate, while those of rats responds to only saccharin sodium. The stimulating effectiveness of 0.3 MEq. chlorides salts in chorda tympani nerve of the monkey is Na \geq Li \geq Ca \geq Mg \geq Sr> NH \geq K, and that of 0.3 MEq. sodium salts is saccharin>F>glutamate> acetate> So \Rightarrow I=N0=Br=Cl. The responsiveness for four basic gustatory stimuli (0.3 M NaCl, 0.3 M sucrose, 0.01 N HCl and 0.003 M quinine hydrochloride) of single chorda tympani fibers was examined. Most of them responded to two or more stimuli, but specific type of fibers, responding to one or two stimuli only, was found to be greater in number in macaque monkey than in rats and hamsters. Probabilities of independent occurrences of responses of the chorda tympani unit to a pair of stimuli were calculated according to the Fisher exact probability test, and their sensitivity to a stimulus was found to be independent of that to the other of a pair. Correlation coefficients between the responses to a pair of stimuli were also calculated in order to see the similarity of neural information among taste stimuli.

1264 REAPPRAISAL OF ADRENERGIC SWEATING IN MAN. <u>Tokuo Ogawa</u>. Dept. of Physiology Niigata University School of Medicine, Niigata, Japan.

Effects of local and systemic administrations of adrenergic agents on human sweat gland activity have been studied by several investigators and a possible role of adrenergic mechanism in sweating associated with muscular exercise has been postulated. However, the mechanism has not been fully assessed and some reported results are controversial. The present study was proposed to re-evaluate the significance of adrenergic sweating in man by systematic investigations. Observations were made on responses of the sweat glands to local and systemic administrations of adrenaline, noradrenaline, isoproterenol, some adrenergic blocking agents and combinations of adrenergic and cholinergic agents in various environmental and physical conditions. Assessments of the responses were made by recording alterations in sweat rate by means of the resistance hygrometry and by determining threshold concentrations of the agents for inducing sweating. The results obtained so far indicate the followings: 1) receptor mechanisms at glandular cells are specific for adrenergic and cholinergic stimuli, respectively; 2) there is no interaction between cholinergic and adrenergic mechanisms; 3) exercise does not affect responsiveness of the sweat glands to adrenergic agents; 4) adaptive changes in the adrenergic sweating mechanism may develop by physical training.

1265 CONTINUOUS RECORDING OF OXYGEN DISSOCIATION CURVE IN VIVO

B. Oeseburg, H.P. Kimmich, F.J.A. Kreuzer, M.L.J. Landsman and G.A. Mook, Lab. of Chemical Physiology, Univ. of Groningen and Dept. of Physiology, Univ. of Nijmegen, the Netherlands.

Oxygen saturation (S_{02}) is recorded in vivo using a fiber optic catheter measuring reflected light. Reproducibility of the method is good, flow artifacts are suppressed effectively (1). Oxygen tension (P_{02}) is recorded at the same site using a modified, teflon covered, catheter-mounted Clark-type electrode (2). Good reproducibility is obtained, flow artifacts being less than 1% of the signal for flow velocities above 5 cm·s¹, using a 6 μ thick teflon membrane. Response time of the two measuring systems could be made to correspond by the use of electronic filters. The S_{02} and P_{02} signals are fed into an X-Y recorder. Using this technique, in vivo dissociation curves have been obtained from the aorta of anaesthetized dogs during artificial ventilation with gas mixtures of different O_2 concentration. During recording, end-expiratory C_{02} , temperature and arterial pH have been checked at frequent intervals. The Bohr effect could be demonstrated.

- Mook, G.A. and M.L.J. Landsman, Fiber optic reflection oximetry. Abstract, this congress, 1971
- (2) Kimmich, H.P. and F.J.A. Kreuzer, Catheter P₀₂ electrode with low flow dependency and fast response. In: Progress in Respiration Research, vol. 3, Karger, Basel 1969, p. 100-110.

1266 ACTION OF CHLORDIAZEPOXID ON CONTRACTILE MECHANISM IN SINGLE FIBRES OF FROG MUSCLE.

H. Oetliker. Inst. of Physiology, University of Berne, Switzerland.

Chlordiazepoxid, 0.4mM, increases twitch tension in a few sec. and this increase is maintained in the presence of the drug for some minutes. Tetanic tension is reduced and cannot be sustained. When tension has fallen to zero during tetanic stimulation, depolarisation by 190mM-K elicits a contracture of smaller size than normal. Recovery from such a contracture, when tested by the method of Hodgkin and Horowicz (1960, J.Physiol. 153, 386 - 403) is diminished. After prolonged recovery in the present of the drug the second contracture is of the same size as the contracture produced 5 min after application of the drug. Both contractures are reduced by about half when compared to the normal. During the recovery period from high K single twitches can be evoked after the same time, in both control and drug experiments. Microelectrode impalements indicate in addition that there is no major slowing and diminution of repolarisation under chlordiazepoxid. Based on the distribution of radio Ca found by Winegrad (1968, J.Gen.Physiol. 51, 65 - 83) and the finding that similar drugs inhibit the sarcoplasmic Ca-pump (Balzer et al. 1968, Naunyn-Schmiedebergs Arch.Pharmak.u.exp.Path. 260, 444 - 455) inhibition of the Ca transport at the junction between the longitudinal and terminal part of sarcoplasmic reticulum could explain the results.

RESPONSES OF SINGLE UNITS IN THE AVIAN TECTUM TO MOVEMENT AND CONTRAST. Juan J. O'Flaherty. Laboratorio di Biologia Spaziale, CNR, Milan, Italy and Max-Planck-Institut für Psychiatrie, Munich, Germany.

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The responses of 124 tectal units to moving and contrasting patterns were studied in paralyzed ducks and pigeons, using long lasting local anesthesia in wounds and pressure points. Receptive fields (RF) determined with moving patterns were roughly circular with diameters varying from 2° (stratum opticum) to 60° (stratum griseum centrale). All units responded specifically and without short-term habituation to motion of light and dark images of various shapes within the RF in one (15%) or several (85%) directions. Discharge rates were maximal at angular velocities ranging between units from 50 to 280°/sec. Tectal elements responded to maximal velocities varying from 200 to more than 2500°/sec. Directional selectivity was in some units velocity dependent. Stimulating patterns had their maximal effect when they subtended angles 1-3° in diameter. Neuronal impulse frequency was independent of the luminance contrast between stimuli and adapting background (LS-LB/LB) within the range .5-50 cd/m². Receptive field size was not affected by changes in the adapting luminance level from .5 to 200 cd/m². Response to flashing spots was on-off in the entire receptive fields and habituated after two or three trials.

A NEW APPROACH TO THE MEASUREMENT OF CENTRAL VENOUS PRESSURE. E. Ogden, M. K. Wells, M. Anliker and H. Sandler. Ames Research Center, NASA, Moffett Field, Calif., U.S.A. and Stanford University, Stanford, Calif., U.S.A.

It has been demonstrated that the blood flow in arm veins can be arrested by raising the pulmonary pressure through a Valsalva maneuver or by blowing against a resistance. If the venous return from a peripheral vein can be shown to change in a characteristic fashion whenever the pulmonary pressure exceeds the central venous pressure (CVP) by a well defined amount, we would have a non-invasive method of measuring the CVP which could also be used under weightless conditions during space flight. A series of experiments on anesthetized dogs were performed in which the CVP was measured directly by means of catheter-tip manometers. The venous flow in the cephalic vein or the jugular was measured transcutaneously with the help of ultrasound Doppler flowmeters while the pulmonary pressure was raised in a well-defined manner. The flow perturbations produced in the vein by the changes of the pulmonary pressure appear to depend on several hydraulic and mechanical factors, including venous distensibility, the frequency and amplitude of variations in pulmonary pressure, and the resulting changes in the CVP. For a rational validation of the proposed method, we have to develop an understanding of the interdependence of these parameters. Initial results show, for example, that there is a linear relationship between changes in tracheal and CVP for sinusoidal variations in tracheal pressure in the frequencies less than one Hertz. The suggestion to explore this approach was made by Mr. Salvador A. Rositano on the basis of his experiments.

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CARDIOVASCULAR RESPONSES IN AWAKE, CHAIRED BABOONS. Winfried W. Ohm, M.D., and Allen M Scher, Ph.D. Dept. Physiology & Biophysics, Univ. of Washington, Seattle, Wash. 98105 USA. In six baboons (10 to 15 kg), transducers were implanted to continuously monitor left ventricular pressure, blood flow in the aortic arch, brachial artery pressure and heart Mean pressure, mean flow and resistance were computed electronically. Cuffs on the inferior vena cava and descending aorta made it possible to change blood pressure at the aortic and carotid baroreceptors phasically or stepwise. (1) The differences in speed of response to phasic changes of blood pressure were used to differentiate between vagally and sympathetically controlled heart rate changes. The tachycardia following decreased arterial pressure showed longer time lags than the bradycardia following increases of pressure. Sympathetic responses predominated with either pressure change, although there seemed to be some vagal response to increased pressure. (2) Stepwise increase of pressure at the receptors led to a marked fall in heart rate and peripheral resistance. Decreased arterial pressure produced an increased heart rate and resistance, the latter predominating (as a percentage of control). (3) Continuous recording of all variables during the night showed a marked stability of cardiovascular function. After midnight, heart rate and stroke volume fell slightly, the concomitant resistance increase was not always large enough to compensate for the fall in cardiac output, and arterial pressure at times fell slightly. conclude that the baboon's circulatory system is largely controlled by the sympathetic nervous system. (Supported by PHS-NIH grant HE 07746-08 and NASA grant NGR 48-002-083, and by Deutsche Forschungsgemeinschaft grant Oh 23/1.)

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THE ROLE OF pH IN SOLUTIONS OF MS-222: EFFECTS ON SALT AND WATER BALANCE AND ANESTHETIZATION. Eleonore A. Ohr, Dept. of Physiol. State Univ. of NY at Buffalo, Buffalo, NY, USA

Ninety percent of frogs injected with DOCA showed no increase in weight due to uptake of NaCl and H₂O from the bathing medium for several days after anesthetization with tricaine methane sulfonate (MS-222, Sandoz). Also, frogs injected with pitressin showed no response to the injection. Titration of MS-222 solutions yielded a pK_a of 3.6; this is also the pH of solutions usually used to anesthetize poikilotherms. Raising the pH of the anesthetizing solution to 1.7 removed the inhibition of the DOCA response. However, it increased the water permeability of the skin so much that no further increase could be detected with injected pitressin. Raising the pH of MS-222 dissolved in distilled water from 3.7 to 7.7 (neutrality) produces a five-fold reduction in the time required to anesthetize goldfish; reduced induction time was also found for frogs, bullfrogs, and necturi at higher pH. We found that the rate of sedation is not significantly altered if the cation of the titrant is Na⁺, K⁺ or Trizma⁺. Assuming that this rate of sedation is proportional to the rate of MS-222 penetration into the animal, we conclude that the greater rate of sedation at higher pH is not due to anionic MS-222 following increased sodium transport. This suggests that the acidic group of the anesthetic is not on the methane sulfonate, as depicted in published structural formulae, but is the meta amino group on the tricaine molecule itself. Since we found that the blood pH of anesthetized bullfrogs is independent of the pH of the MS-222 solution, this amino group can apparently be neutralized by body buffers.

1271 SENSORY TRANSMISSION IN THE HUMAN THALAMUS. <u>C. Ohye and H. Narabayashi</u>. Neurological Clinic, Tokyo and Dept. of Neurosurgery, Univ. of Gunma, Gunma, JAPAN

During the stereotaxic surgery in 50 cases, the extracellular spontaneous and induced activity was recorded in and around the specific sensory nucleus (VP) with a microelectrode (tip diameter: 5-10µ, resistance about 100KA). In our anterolateral to posteromedial approach in micron steps, we found different unitary activity almost every 200µ in VP area. In anesthetized patients, majority of the cells were discharging in rhythmic or irregular bursts (75% of 56 cells). These cells discharging in bursts never responded to peripheral natural stimulation. In awake patients, the continuous spontaneous discharges were predominant and some of them responded to the peripheral natural stimulation of a certain modality. Monitoring the local EEG pattern, we found that the same peripheral stimulation provoked more spikes in the active phase. The general anesthesia (barbiturate) reduced the extent of peripheral receptive field, while the thalamic response was almost the same.

RECOVERY FROM ANOXIA OF DIFFERENT DURATION IN OLFACTORY CORTEX SLICES OF GUINEA PIG.
Y.Okada, I.J.Bak and R.Hassler. Dept.Neuroanatomy, Max-Planck-Institut for Brain
Research, Frankfurt/M.-Niederrad, Germany.

Olfactory cortex slices (250 µ) were incubated in oxygenated glucose-Krebs-Ringer's medium. Postsynaptic potential (N-wave) was recorded from piriform cortex during the stimulation of lateral olfactory tract. They were transferred to oxygen-free mineral oil bath (38°C) for 1-30 min and subsequently reoxygenated for 20 min in the previous medium. With 1-15 min anoxia and 20 min reoxygenation, ATP and CrP recovered to 80-100% of the control level. Complete recovery in the amplitude of N-wave was observed in the slice with 1-10 min anoxia and 52% of recovery was seen in slices with 15 min anoxia, though the N-wave was completely blocked during anoxia. With 30 min anoxia ATP recovered only to 43% and CrP to 60% but no recovery in N-wave. After 30 min anoxia one group of slices was reoxygenated for 60 min adenosine and creatine in incubation medium. Though ATP and CrP returned to 90-95%, the recovery of N-wave was not observed. - This suggests that the block of N-wave due to anoxia could not only be attributed to inability of slices to replenish the high energy compounds and may indicate some other constituents necessary for preservation of synaptic potential. The relation to the electron microscopical preservation of the slices is to be discussed.

LUNG VOLUME AND UNEVEN DISTRIBUTION OF PERMEABILITY FOR CO IN THE HUMAN LUNGS. T.Okubo, K. Takahashi, and T.Nakamura. First Dept. of Internal Med., Tohoku Univ. Sch. of Med., Sendai, JAPAN.

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To investigate the uneveness of permeability for carbon monoxide in the lungs, we measured the disappearance of CO at various lung volume in five healthy men using single breath methode during both air and oxygen breathing, varying breath-holding time from 2 to 50 second. As results, (1) three of five subjects showed straight decay on semi-logarithmic plot at TLC level and uneveness became more evident as lung volume decreased. (2) Such uneveness at low lung volume were exaggerated when endoexpiratory gas samples were used. In such cases, the lung volume could be divided into three compartments according to their permeability of which highest reached up to 30 cc/mmHg. min. l. (3) Dividing the lung volume into two compartments at FRC level, CO decay were analysed for the seperation of menbrane component and pulmonary capillary blood volume factor. One of the compartments has 1/3 of the lung volume of which DM/VA and Vc/VA were ranged 20-30 and 80-100, respectively, and another has 15-20 and 10-15 of the values of DM/VA and Vc/VA. It can be concluded that the compartment of higher permeability presumably plays an important role on the pulmonary gas exchange.

BLOOD URIC ACID LEVELS AS AN INDICATOR OF THE DEGREE OF HYPOXIC DAMAGE IN ENDOTOXIC SHOCK IN THE DOG. S. Okude, W.B. Jolley, L.L. Smith, and D.B. Hinshaw. Dept. of Surgery, Loma Linda University School of Medicine, Loma Linda, California, U.S.A.

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Increased serum uric acid levels in the dog has been reported during hemorrhagic shock. This uric acidemia appears to reflect purine catabolism during periods of severe hypoxia. It was felt, therefore, that the phenomenon might be observed following endotoxic shock. Twenty dogs were lightly anesthetized with sodium pentobarbital and were given E. coli endotoxin (Difco) systemically in 10 dogs and locally in the mesenteric arterial circulation in an additional 10 animals. Hemodynamic and biochemical measurements were made during shock. Blood samples were taken prior to endotoxin administration, and at hourly intervals for the measurements of plasma uric acid levels. In an attempt to minimize error by the conventional colorimetric technique uric acid concentration was determined chromatographically on a Varian high pressure liquid chromatograph. This technique is more sensitive and more specific. The plasma uric acid level increased (expressed as % of baseline) following systemic endotoxin. These values were: 1 hour=1155, 3 hours=805, and 6 hours= 585. The local administration of endotoxin into the mesenteric circulation also caused an increase in the mesenteric venous uric acid: the relative uric acid concentration as % of baseline was: 1 hour=245, 2 hours=1025, 3 hours=1615, and 4 hours=2404. The increase in plasma uric acid concentration paralleled the severity of the shock state. Preliminary observations indicate that this test may also have the same significance in acute circulatory disturbances in man. (Supported by NIH Grant #HE 04639).

"LEARNED RESPONSES" IN "REWARD CENTERS" AND OTHER SUBCORTICAL AREAS OF RAT BRAIN. J. Olds. Div. of Biology, California Institute of Technology, Pasadena, Calif., U.S.A.

1275

Changes in single unit firing rates in response to auditory stimuli were recorded automatically from chronic animals during Pavlovian alimentary conditioning experiments. A canvass was made to find areas yielding short latency new responses with a view to locating sites where the brain CR's would be at primary foci rather than at secondary centers which merely conveyed but did not originate new messages. A surprisingly large number of pointS yielded new responses of very short latency. New responses followed the CS by about 20 msec at points in the colliculi, non-specific areas of midbrain and thalamus, and in some parts of the neocortex and hippocampus; but they were particularly frequent in lateral hypothalamic and ventral tegmental regions which have been thought of as "revard centers." Besides having short latency, new responses in these areas appeared very early in the series of learning trials; whereas short latency new responses did not appear in hippocampus until long after the animal exhibited overt CR's. It was appealing to suppose that early in learning, subcortical centers might temporarily connect sensory and motor pathways; pathways which later in learning (after the new behaviors had become to some degree automated) would be connected via similar mechanisms in hippocampus (freeing the lower systems for re-use in relation to newer problems).

ADRENERGIC AND CHOLINERGIC ACTION ON BEHAVIOR AND UNIT ACTIVITY DRIVEN BY BRAIN REWARD.

M. E. Olds and M. Ito. Division of Biology, California Institute of Technology, Pasadena,
Calif., U.S.A.

Unit activity driven by positively reinforcing stimuli during self-stimulation (SS) behavior has been observed in the cingulate cortex and in the hypothalamus. In the cingulate, the response was a "driven" spike (Ito, M. and Olds, J., 1971). In the hypothalamus, the response was either a similar driven spike or a period of suppression of spontaneous activity. This driven neuronal activity afforded the opportunity to study the action of drugs with adrenergic and cholinergic central effects simultaneously on SS and at sites functionally linked to the rewarding regions. The subjects were chronic rats with microelectrodes for recording and macroelectrodes for brain reward. Two tests were given each animal. In the first, SS was depressed by tetrabenazine and reinstated by d-amphetamine. In the second, SS was depressed by physostigmine and reinstated by scopolamine. Tetrabenazine abolished the driven response in the cingulate but the effect was less in the hypothalamus, and it had no effect on the inhibitory response driven in the hypothalamus. Reinstatement of the driven response after d-amphetamine administration lagged behind reinstatement of the SS behavior. Physostigmine inhibited SS behavior but had no effect on the driven spike or the driven suppression either in the cingulate or the hypothalamus. Reinstatement of SS behavior by scopolamine was not reflected in any modification of the driven response. These results suggest a more direct involvement of adrenergic mechanisms and only indirect involvement of cholinergic mechanisms.

JUNCTIONAL MEMBRANE PERMEABILITY AND DIVALENT CATIONS. Gilberto M. Oliveira-Castro. Cell Physics Lab., Dept. of Physiol., Col. of P & S. Columbia Univ., New York, N.Y. USA.

Through a hole in the membrane of one cell, coupled cells of Chironomus salivary gland were equilibrated with media of various divalent cation concentrations. Electrical conductance and permeability to fluorescein (330 MW) of the junctional membrane were monitored. In divalent cation-free media, junctional membrane conductance and permeability to fluorescein are high, as they are in the normal unperforated cell system. In presence of alkaline earth or other divalent cations, junctional conductance is depressed, effectively interrupting ion flow between cells (uncoupling). Minimum concentration for uncoupling with Ca ions is $4-8 \times 10^{-5} M$. Relative potencies of the alkaline earth ions are Ca: Mg: Sr: Ba = 1:0.11:0.016:0.008. The uncoupling is reversed during repolarization of the cells with inward current in divalent cation-free media, but not in divalent cation-containing media. The divalent cations also effectively block junctional passage of fluorescein. Mn parallels the action of the alkaline earth ion on junctional conductance.

1278 DETERMINATION OF THE MITOCHONDRIAL REDOX POTENTIAL. Christian Olsen. Inst. of Physiology, University of Aarhus, Denmark.

In the perfused rat liver it has been shown, that the lactate/pyruvate ratio (L/P) in the blood, reflects the cytoplasmatic NAD/NADH ratio (Schimassek 1962). The present experiments were undertaken to demonstrate, whether the β -hydroxybutyrate/acetoacetate ratio $(\beta$ -HB/Ac) in the blood reflects the mitochondrial NAD/NADH ratio. 1. Rising the β -HB/Ac ratio 5 times in the blood entering the liver by injection of β -HB to the reservoir did not change the ratio in the blood leaving the liver. 2. When the ratio of NAD/NADH in the liver was changed by hypoxia or by ethanol, both L/P and β -HB/Ac ratio increased. The ratios increased with the same velocity. 3. The calculated redox potential difference across the mitochondrial membrane was not significantly altered by hypoxia but was significantly (P<0.001) lowered by ethanol. This change in redox potential difference was independent of the redox potential difference before addition of ethanol. It is concluded that the mitochondrial ratio of NAD/NADH might be calculated from the β -HB/Ac ratio in the blood leaving the perfused rat liver. The β -HB/Ac and L/P ratio yields information on the redox potential across the mitochondrial membrane.

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CENTRAL REGULATION OF ADH-RELEASE IN THE CONSCIOUS GOAT. K. Olsson, L. Eriksson and O. Fernández. Dept. of Physiology, Royal Veterinary College, 104 05 Stockholm, Sweden.

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The antidiuretic response to intracarotid infusions of hypertonic sodium salts and of sucrose in the hydrated dog suggests that hypothalamic "osmoreceptors" regulate the release of antidiuretic hormone (ADH). However, hypertonic solutions of di- or monosaccharides infused into the 3rd ventricle of the goat have no antidiuretic effect, although similar infusions of hypertonic NaCl effectively release ADH. Therefore it appeared of interest to study the effect of the same osmotic stimuli when applied outside the blood-brain barrier in the hydrated goat. Vinyl catheters were implanted into the carotid artery via its facial or superficial temporal branches, making it possible to infuse various solutions into the blood supply of the brain in the conscious undisturbed animal. Prolonged (10–30 min, 1.5 ml/min or 2 ml/min) infusions of hypertonic solutions of NaCl (0.5 M or 1 M) and of sucrose, fructose, glucose and galactose (1 M or 2 M) were performed. The infusions of hypertonic NaCl or sucrose invariably turned renal free water clearance into negativity for at least half an hour, indicating a release of ADH. Of the monosaccharides only fructose gave a similar antidiuretic response. This suggests that brain-barrier systems are of greater importance in the osmotic regulation of ADH-release than the membrane permeability of certain cells in the hypothalamus. This work was supported by the Swedish Medical Research Council (project nr K71-14X-3392-01A and B71-99F-3054-02).

ADENOSINE TRANSPORT IN CANINE MYOCARDIUM. Ray A. Olsson. Walter Reed Army Institute of Research, Washington, D. C. 20012, USA.

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The importance of myocardial cellular uptake of adenosine as a mechanism for regulating extracellular levels of this coronary vasodilator metabolite was assessed in anesthetized, open-chest dogs. Adenosine uptake by the heart appeared to follow Michaelis-Menten kinetics, Vmax 4.9 ± 0.7 (SEM) nmole/g left ventricle per minute and Km 12.0 ± 2.4 (SEM) μ M. Uptake was inhibited by intracoronary infusions of 6-methylaminopurine riboside or 6-mercaptopurine riboside, and was stimulated by intracoronary infusions of insulin. Adenosine uptake was not influenced by 2'deoxyadenosine, uridine, ouabain, or dipyridamole. These results are consistent with carrier-mediated transport of adenosine. The rate of transport into the myocardial cells appears to be sufficiently rapid to be an important factor in regulating cardiac adenosine levels.

ANALYSIS OF ALVEOLAR GAS EXCHANGE IN THE STEADY AND UNSTEADY STATES.

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In the classical alveolar gas exchange equations, the cyclic pattern of ventilation is reduced to a continuous gas flow. Consequently the interesting periodic variation in alveolar gas tensions and fluxes cannot be studied. An additional limitation of this system of analysis and of the computer techniques based on it is that they apply only to steady state conditions. A program we have developed for use on an EAI 580 analog computer (64 amplifiers plus logic) allows us to predict mixed venous blood composition in the steady or unsteady state on the basis of inspired gas, lung volume, overall ventilation and perfusion, human blood dissociation curves (with Bohr and Haldane effects), tissue metabolism, and body gas stores. This mixed venous blood serves as an input parameter in following alveolar gas composition in steady or unsteady states in an individual element in which gas volume and its periodic changes, tissue CO_2 dissociation curve, and perfusion can be set at will. We have found this model particularly useful in studying the effects of ventilatory pattern \underline{per} se and for predicting the important gas tension changes that occur during uptake and elimination of soluble anesthetic gases.

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1282 GREATER PENTOSE PATHWAY (PP) ACTIVITY IN ISOLATED PERFUSED LUNG (IPL) THAN IN TISSUE SLICE (TS) OF RAT LUNG. John J. O'Neil and Donald F. Tierney. Dept. Physiol. UC San Francisco and Dept. Med., Harbor Gen. Hospital, UCLA School of Med., Torrance, Calif. 90509, USA.

The PP of Glucose (G) exidation contributes reduced nucleotides which are probably used for synthesis of surface active material (SAM) and other cellular components. In addition these reduced nucleotides may have an important role in the lung to maintain a normal redox state despite the presence of a high PO₂ or other oxidants. Although TS have been used to study lung metabolism the IPL has the following advantages: 1) Synthesis and secretion of SAM and tissue PO₂ may more accurately reflect the in vivo conditions in IPL since it is ventilated. 2) Substrate delivery is from capillaries and not from the edge of TS. 3) Edema formation, changes of lung compliance and vascular resistance can be observed. 4) Ventilation and blood flow can be controlled. 5) Less tissue damage occurs in IPL since it is intact and not sliced. Using TS and IPL we compared the metabolism of 1-\frac{14}{C}-G, 6-\frac{14}{C}-G and 1-\frac{14}{C}-palmitate in rat lung. We used the same medium, temperature, and ratio of medium volume to lung weight for the TS and IPL. The TS and IPL produced approximately equal ammounts of \frac{14}{C}O_2 from 6-\frac{14}{C}-G (n=\frac{1}{4} IPL, 10 TS) and 1-\frac{14}{4}C-palmitate (n=\frac{1}{4} IPL, 10 TS). The \frac{14}{C}O_2 from 1-\frac{14}{C}C-G by IPL (n=\frac{1}{4}) was more than twice that from TS (n=\frac{10}{4}). The PP in TS and IPL could be stimulated to approximately equal activities (6X in TS, 2X in IPL) by addition of the herbicide Paraquat (5x10-\frac{14}{4}). The greater activity of PP in IPL may be related to greater synthesis of SAM or to a different redox state. (Supported in part by USPHS grants 12020, CM 00927 and Research Career Development Award HE-10,637.)

CHARACTERISTICS OF THE CHEMORECEPTOR NEURON IN THE RAT HYPOTHALAMUS
Y. Oomura, T. Ono, M. Sugimori, T. Nakamura, D. Gawronski and H. Ooyama
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Glucoreceptor neurons in the ventromedial hypothalamic nucleus (VMH) and the lateral hypothalamic area (LH) of rat respond to changes in blood glucose, and direct microapplications of glucose increase unit discharge rates in VMH and decrease them in LH. A series of experiments was conducted to determine whether actual incorporation of glucose through the receptor membrane or specific binding of glucose to the receptor membrane is essential. to activate the glucoreceptor mechanism. Thus, the combined effects of glucose, glucose and insulin, and several glucose analogs vere studied using multibarreled microelectrode techniques. Discharges of single glucoreceptor neurons in rat VMH increased significantly in frequency when glucose and insulin were applied simultaneously, but did not change with insulin alone. Glucose analogs, 2-deoxy-D-glucose, 3-0-methylglucose, and goldthioglucose either had no effect on activity or inhibited the glucose effect. When a glucose analog and insulin were applied simultaneously, the firing rate decreased. These results indicate the importance of glucose incorporation into the cell through the receptor membrane for the activity of the glucoreceptor neuron.

ANTIGEN-ANTIBODY REACTION IN THE SATIETY CENTER OF THE RAT HYPOTHALAMUS Y. Oomura, T. Ono, M. Sugimori, T. Nakamura and H. Ooyama Dept. of Physiology, Faculty of Med., Kanazawa Univ., Kanazawa, Japan

The rat ventromedial hypothalamic nucleus (VMH) contains neurons which respond specifically to blood glucose. These neurons receptive sites may have a particular membrane protein configuration for which a specific VMH antibody may be produced in rabbit serum. Microapplication of this antibody may be expected to inhibit the activity of VMH neurons through a specific antigen-antibody reaction. After production and identification of this antibody in rabbit serum, antibody was applied electrosmotically to rat VMH neurons through multibarreled electrodes. With fresh antibody unit dischanges briefly increased in rate then suddenly ceased irreversibly. When the antibody was not fresh, activity decreased or ceased for a considerable period but eventually returned to the original level. Two-thirds of the VMH neurons which responded to glucose applications were inhibited in this manner. Normal rabbit serum and antibody for rat caudate nucleus did not affect VMH neurons, but caudate antibody did inhibit unit activity in caudate neurons. The different actions of fresh and non-fresh antibody might be due to the existence of complement which is easily destroyed. These results provide one more step toward clarifying the specific membrane characteristics of the chemoreceptive neuron.

A STOCHASTIC MODEL FOR VISUAL TIME-DIFFERENCE DETECTION. M.W.M. Oostenbrug and J.W. Kuiper Natuurkundig Laboratorium, Biophysical Department, University Groningen, Netherlands.

1285

Time differences between short light flashes form the stimulus in psychophysical experiments in which a first short flash is presented to one eye and a second flash to the other. The detectability is determined in yes—no experiments and in discrimination situations and the results are studied by means of detection theory. An analytical stochastic model is presented which tentatively establishes a connection between our experiments and experiments on flicker-fusion as described (a.o.) by Veringa and Kelly who have deduced from them a transfer-function for the entire visual system. In the high-frequency range the performance of this transfer-function may however, according to Brindley, be wholly located at a periferal (i.e. retinal) level. We have used the flash responses as deduced from this function as an input to our model. These analog responses have been interpreted in a stochastic way; they modulate the parameter of a time-dependent poisson process which must generate the spike signal. The spike signals from each eye then enter an excitation-inhibition-coincidence network whose spike output is counted in order to yield a time-difference value. This value is then compared to a criterion value which is set by a mechanism independent from the network. This model can generate detection and noise characteristics that can be fitted to the experimental results by no more than two independent parameters.

EXAMINATION OF ANTISERUM SPECIFITY PRODUCED AGAINST HOMOGENATE OF CAT CEREBRAL CORTEX. A. Orosz, A. Falus, J. Gergely, Emilia Madarász and G. Adám. Dept. of Comparative Physiology, Eötvös Loránd University, Budapest, Hungary.

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Rabbits have been immunized with saline homogenate of phospholipid-free cat cerebral cortex incorporated with Freund-adjuvant. The obtained antiserum has been absorbed with cat serum as well as with liver and kidney extracts. Immunochemical examinations using cat visual cortex antigen revealed the following: 1. Of different subcellular fractions /nuclear, myelin, mitochondrial, synaptosomal, synaptic vesicles, microsomal and soluble/ antigen was found only in the soluble fraction. 2. Of the peaks obtained in course of DEAE-cellulose chromatography of the soluble fraction only one peak contained antigen; its polyacrilamide disc-bands also showed discrete reactions with the antiserum. 3. After treatment of the subcellular fractions with Triton X-100 antigen could be observed only in synaptosomal fraction the former differed from the soluble antigens; after osmotic treatment no immune reaction has been experienced. The effect of the brain specific antiserum on cortical evoked potentials has been examined in cats.

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STUDY OF CHOLINERGETIC TRANSMISSION IN THE COLD-BLOODED ANIMALS RETINA. M.A.Osrovsky, P.P.Sack. Inst.of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences, Moscow, USSR.

(I) Acetylcholine applied to isolated retina evokes an impulse activity, which depends on the state of photoreceptors (light and dark adaptation, damage of outer segments). The pharmacological analysis shows that the reaction is specific. (2) The cholinolitic and cholinomimetic drugs have a specific influence on the intacellularly recorded light and dark potentials of horizontal cells, which are directly connected with the photoreceptors. (3) By means of histochemical methods (light and electron microscopy) it was shown, that acetylcholinesterase is localised on the structures of the outer synaptic layer. The results obtained do not exclude the possibility of the participation of some other mediators in the synaptic processes in the retina.

1288 EFFECT OF VAGAL BLOCK ON RENAL SYMPATHETIC OUTFLOW DURING NORMOCAPNIA AND HYPERCAPNIA.

Norbert T. Ott and John T. Shepherd. Mayo Foundation and Mayo Graduate School of Medicine, Rochester, Minn. 55901, U.S.A.

Six rabbits were anesthetized with pentobarbital and artificially ventilated; both carotid sinus and aortic depressor nerves were cut. One kidney was perfused at constant flow by a roller pump with autologous blood at 37 C. One outlet from the pump passed directly to the kidney; the other entered a 150-ml loop which constituted a reservoir of blood of varying PCO2. Switching outlets permitted perfusion of the kidney with blood of the same or different CO2 content from that traversing the systemic circulation. Vagal cold block (VCB) during systemic and local normocapnia increased renal perfusion pressure by 17 mm Hg (SE, 4.2); VCB when the kidney was perfused with hypercapnic blood increased the perfusion pressure by 27 mm Hg (SE, 8.5). VCB during systemic hypercapnia and kidney perfusion with hypercapnic and with normocapnic blood resulted in increases in perfusion pressure of 69 (SE, 5.3) and 62 (SE, 9.6) mm Hg, respectively. In another 5 rabbits, renal sympathetic activity was recorded. VCB in normocapnia (end-tidal CO2, 3%) increased spike activity from 100% to 134% (SE, 11.6). Increasing CO2 tension (end-tidal CO2, 9%) augmented the neuronal activity to 202% (SE, 25.6); VCB potentiated this response to 320% (SE, 37.1). Thus, vagal afferent activity, as revealed by vagal block, caused a greater decrease in sympathetic nerve activity to the kidney in hypercapnia than in normocapnia. This decrease was not due to local effects of CO2.

VASCULAR RESPONSES TO K+ IN HYPERTENSIVE RATS. <u>H.W. Overbeck and D.W.J. Clark</u>, Departments of Physiology and Medicine, Michigan State University, East Lansing, Michigan, U.S.A., and Wellcome Medical Research Institute, Dunedin, New Zealand.

A defect in vascular K+ metabolism might underlie the abnormal vasoactivity of hypertension. Therefore, vascular responses to infusions of K+ were studied in the isolated, pumpperfused (blood, 1 ml/min) hindlimb vascular beds of 25 genetically hypertensive (GH) rats from the N.Z. colony, 18 renal hypertensive (RH) rats with one renal artery clipped, and 17 sham-clipped normotensive (N) rats, under IV chloralose and pentobarbital anesthesia. Innervated and denervated preparations were used. Paired equivolume 4-minute infusions of isotonic NaCl (control) and isotonic KCl, 0.012, 0.02, or 0.03 ml/min were made into the upstream pump tubing. Pump perfusion pressure was monitored. Measured limb arterial plasma $[K^+]$ ranged from 11.4 to 12.0 mEq/1 during infusion of 0.03 ml/min KCl. In response to each dose level of K+, statistically significant (P < .01, paired Student t test) decreases in limb resistance occurred in each group. At each dose level in all rats there was a significant linear correlation (P < .05) between initial limb resistance and magnitude of response. Analysis of covariance indicated that responses in RH rats to the two higher dose levels were decreased when compared to responses in GH and N rats (P < .01). In contrast there were no significant differences between responses in GH and N rats (P>.1). We conclude that K+ decreases limb vascular resistance in rats, and that the magnitude of response to K^+ may be decreased in RH rats, as we have found in RH dogs and essential hypertensive men. In contrast, the response to K^+ in GH rats is apparently normal.

1290 IONIC MECHANISM OF INHIBITORY POSTSYNAPTIC POTENTIAL OF CRAYFISH STRETCH RECEPTOR CELL. S.Ozawa and K.Tsuda. Dept.of Neurophysiol., Inst.of Brain Res., Univ.of Tokyo, Tokyo, Japan.

Two microelectrodes filled with 2M-Kcitrate were penetrated into a stretch receptor cell of crayfish. In normal Van Harreveld solution the reversal potential of IPSP evoked by stimulation of the accessory nerve was close to the resting potential, while the equilibrium potential of K was 8 mV more negative than the resting potential. After the cell was washed with Cl-free solution containing GABA and then with Cl-free solution without GABA, the IPSP was almost abolished. Under this condition conductance increase by application of GABA was only 5-6 % of that in normal solution. When K of external solution was decreased to one-fourth, the resting potential first became 18-22 mV more negative, and then gradually depolarized. At this stage of depolarization the reversal potential was much more negative than the resting potential. But it was not so different from the peak value of the resting potential. This phenomenon may be explained without assuming the permeability increase of K therefore it is concluded that the current generating IPSP is mainly carried by the movement of Cl-.

ISOLATION AND IDENTI ICATION OF FOUR COMPONENTS IN THE b WAVE OF THE ELECTRORETINO-GRAM (ERG) OF THE CAT. Pablo Pacheco and Ricardo Fuentes. Inst. de Investigaciones Biomédicas, UNAM. Apdo. Postal 70228, México 20, D.F. México.

1291

A complex, multiple wave ERG was evoked in cats by a small spot of light (2.3 mm diameter) placed 2 mm from the cornea and recorded \underline{ac} (80 Hz high and 50 Hz low frequency filters). In nembutal-anesthetized animals (approx. 20 mg/kg b.w.) positive components of the ERG consisted of four waves. Deepening of the anesthetic level (approx. 10 mg/kg b.w.) provoked a reduction in amplitude of the first two waves and increments in latency of the last two waves. Changes in position of the spot, 1 mm each time, from the periphery to the center of the eye, provoked progressive increments in amplitude of the first waves and reductions in latency of the late waves. Low intensities of the spot resulted in reduced amplitudes and increased latencies of the four waves. High frequencies of the spot reduced the amplitude of the first waves and the latency of the late waves. These results suggest that both group of waves represent the activity of different group-cells in the retina which are triggered by different excitatory processes.

This research was supported by THE FUND FOR OVERSEAS RESEARCH GRANTS.

45Ca-UPTAKE OF ISOLATED GUINEA-PIG AURICLES AT REST, DURING EXERCISE AND UNDER THE INFLUENCE OF SPECIFIC INHIBITORS OF EXCITATION-CONTRACTION COUPLING. O.Pachinger, J.Janke, W.Jaedicke and B.Hein. Physiological Institute, University of Freiburg, Germany.

1292

Isolated guinea-pig auricles were suspended at 30°C in Tyrode solution containing 1.8 mM 45-labelled Ca. At rest, the percentage of extracellular activity incorporated into the myocardium was as follows: 34% within 2.5 min, 44% within 5 min, 60% within 10 min. Upon stimulation at 120/min, the corresponding values rose to 43%, 54% and 71% respectively. Specific inhibitors (1,2) of excitation-contraction coupling (verapamil or D 600, a methoxy-derivative of verapamil) in a dose which decreased isometric tension by 90%, reduced the radiocalcium uptake to resting level or even lower. Prenylamine acts in a similar way. Conversely, isoproterenol or K-strophanthin, which neutralize the effects of verapamil and D 600 on contractility, restored the Ca incorporation into the stimulated auricles. The above effects were accentuated by lowering the Ca in the Tyrode solution to one half.

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A TOPOGRAPHICAL STUDY OF ANTIDROMICALLY ACTIVATED RUBRO/SPINAL CELLS IN THE CAT. Y. PADEL, A. SMITH, J. ARMAND. Departement de Neurophysiologie Générale. I.N.P. -C.N.R.S., Marseille, France.

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Extracellular recordings were made from a total population of 215 red nucleus cells antidromically activated by stimulation of the rubro-spinal tract - 98 of these cells sent axons to cervico-thoracic segments of the cord and 117 cells sent axons to lumbo-sacral segments.

(1) The density of rubro-spinal neurons is considerably greater in the posterior red nucleus than in the anterior region. The cervical neurons occupy a dorsomedial position in the nucleus. The cells are very medial in the posterior portion and more dorsal in the anterior region. Lumbar neurons are found in the ventro-lateral part of the nucleus and are particularly lateral in the posterior portion and become more ventral in the anterior portion. These two zones have some overlap especially in the anterior regions. The results confirm the anatomical findings of POMPEIANO & BRODAL.
(2) The distribution of conduction velocities for rubro-spinal fibers, calculated for the cervical lumbar segment, yielded a range between 12 m/s and 150 m/s with a mean of 83 m/s. The largest fibers are found principally in the posterior red nucleus and the smaller fibers in the middle and anterior regions of the nucleus.

THE INFLUENCE OF PRESSURE AND GAS COMPOSITION ON WATER VAPOR DIFFUSION. C.V. Paganelli,
A. Ar, and E. H. Lamphier. Dept. Physiol., St. Univ. of N.Y. at Buffalo, Buffalo, NY, USA.

Diffusivity in a binary system of gases varies with pressure, temperature, and composition. Since gas and water vapor exchange of avian eggs depends on diffusion through the porous shell, we have used intact, unfertilized chicken eggs to measure the effect of ambient pressure (PB) and gas composition on water vapor diffusion. Eggs were placed in vented dessicators containing either silica gel or KOH, and water loss via diffusion measured by periodic weighings. Water loss per egg at 1 ATA and 25°C.averaged 273 ± ¼6 (s.d.) mg day-1; the corresponding water vapor permeability is 2.5 x 10-6 cm³ (STP) sec-1 cm-2 (mmHg)-1. In experiments done at 5 values of PB between .13 and 1 atmosphere absolute (ATA), water loss rate rose linearly with 1/PB, as predicted by kinetic theory. Below .13 ATA, water loss rate increased less rapidly than 1/PB, probably because of evaporative cooling and consequent water vapor pressure reduction within the egg. Water loss rates at 2 and ¼ ATA were reduced respectively to .65 and .35 x the rate at 1 ATA. Diffusive water vapor loss in He at 1 ATA was about 2.¼ x greater than in N2 under the same conditions. The theoretical ratio is 1.83, based on kinetic theory. The discrepancy is perhaps a reflection of non-ideal behavior of water vapor in our binary diffusion system. (Supported in part by the U.S. Office of Naval Research and the U.S. Air Force.)

1295 CENTRIFUGAL CONTROL OF OLFACTORY INPUT IN FOOD SATIATED OR DEPLETED RATS. J. Pager,

I. Giachetti, A. Holley, J. Le Magnen. Lab. of Electrophysiology, Claude Bernard

Univ., 69, Lyon, France and C.N.R.S., Collège de France, Paris.

The olfactory bulb is submitted to a centrifugal inhibition. Could this inhibition selectively control the transmission of afferent inputs in close connection with definite physiological conditions, especially nutritional ones? This hypothesis has been tested by recording the integrated multiunit activity of mitral cells in unanesthetized rats, stimulated by their usual food odour, or amyl acetate, or citral. The animals were either food satiated or food deprived; some of them had received a postprandial insulin injection. In satiated rats, all the above odours decreased or unchanged the mitral activity. On the contrary, during natural or insulinic depletion, the food odour induced a significant increase of electrical activity, contrasting with the unchanged or decreased response to non alimentary odours. These findings appear to support the following conclusions: at such a peripheral level as mitral cells, the olfactory input is subjected to a selective centrifugal control depending on the internal physiological conditions; the selectivity of this control is determined by the relevance of the odours to the animal behaviour rather than by their physico-chemical properties.

INTRACELLULAR pH: DIRECT MEASUREMENT IN RAT AND CRAB MUSCLE IN VITRO. M. Paillard, J.-D. Sraer, F. Leviel, M. Claret. I.N.S.E.R.M., Hôpital Tenon, Paris, France.

Direct intracellular (I.C.) pH determinations in rat leg muscle in vivo by Carter and al. support a passive H ions distribution when Caldwell's results obtained in crab muscle favor an active process. To investigate this difference single pH microelectrodes as described by Carter were used to record I.C. pH values in both preparations. I.C. pH recorded near the surface of both preparations agreed with Donnan equilibrium and each new equilibrium was reached almost instantaneously when incubation medium (I.M.) pH or membrane potential (M.P.) was changed. I.C. pH recorded in a deeper zone, on the opposite did not agree any more with Donnan equilibrium (6,80 - .10 SD in rat muscle, and 6,84 - .12 SD in crab muscle, when I.M. pH = 7,40) and these values were poorly influenced by I.M. pH or M.P. modifications. These apparently contradictory results could be explained in two ways: 1- H ions are distributed according to Donnan equilibrium as suggested by Carter, and the deep values could be explained by a lack of equilibration between interstitial fluid and I.M. in rat muscle. That interpretation, however, requires the giant fibre of crab to be a non single unit. 2- H ions are not distributed according to Donnan equilibrium and a systematic artefact could explain the superficially recorded I.C. pH values if the length of the microelectrode sensitive tip exceeds 20 µ. It may be pointed out that deeply recorded values are in agreement with both Caldwell's direct determinations in crab fibre and several indirect ones in rat muscle by the D.M.O. method.

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THE INFLUENCE OF BLOOD GAS TENSIONS AND HAEMATOCRIT ON BLOOD FLOW THROUGH A CAPILLARY NETWORK. M.C.F.Pain, J.F.Cade, D.Bucens. Respiratory Unit, Royal Melbourne Hospital, Melbourne, Australia.

1297

Evidence of changes in the rheological properties of blood induced by alterations in haematorit, oxygenation and acid-base state has been sought by studying the induced alterations in pulmonary vascular conductance in an isolated canine lung preparation. The results obtained from 15 preparations judged to be technically satisfactory may be summarized thus: Haematocrit: Vascular conductance decreased linearly with rising haematocrit (range studied = 20% to 92%) such that increasing the haematocrit of blood from 40% to 80% reduced the vascular conductance to one third of its original value. Studies with hypoxaemia and respiratory acidosis (mean PO2 30 mm Hg; mean PCO2 82 mmHg) and Hypoxaemia and lactic acidosis (mean PO2 32; mean pH 6.93) did not reveal any difference in the rate of change of conductance with haematocrit variation compared with blood of normal blood gas composition. We concluded that, within the range of value studied, there was no evidence to suggest that the viscosity of blood at a given haematocrit is increased under conditions of hypoxaemia lactic acidosis or hypercapnia.

EFFECT OF EMETINE-HCl ON THE ELECTROMECHANICAL PROPERTIES OF HEART MUSCLE. M. J. Pak, B. W. Swanton and M. Medow. Dept. of Biol. Sci., Oakland Univ. Rochester, Mich. USA

1298

The value of emetine as an amebicidic therapeutic agent has been appreciated since 17C, but its recent use has been curtailed by increased awareness of its toxic actions especially to the heart. Numerous in vitro experiments showed that it affects; myocardial metabolism, protein synthesis, and impulse conduction. This investigation involves the effect of emetine on the electrophysiological and mechanical parameters of isolated ventricle strip. At therapeutic concentration, emetine reduced the amplitude of the peak isometric twitch tension as well as the maximum rate of isometric tension development. The reductions were seen at all stimulation frequencies but more pronounced at lower ones. The threshold for the excitation increased with emetine. After 40 Min. exposure, stimulation intensity had to be increased to 10 fold of control level. After a prolonged exposure a mechanical response could still be obtained with massive field stimulation but the response became graded. The observed reduction in tension was accompanied by the progressive shortening of the plateau phase of action potential. An interesting phenomenon observable after a prolonged exposure was the appearance of two types of action potential; one with longer duration and one with much shorter duration. Train of each type alternated without any obvious regularity. Corresponding mechanograms showed tension alterans consistent with each type of action potential. At a higher concentration, the plateau phase was completely abolished and action potential assumed a spike form.

CONTRIBUTION TO THE BIOCHEMICAL STUDY OF EXPERIMENTAL RICKETS. M. Palade, A. Brătianu, G. Vătafu, B. Herşcovici, E. Papp, E. Dughir. Faculty of Medicine, Jassy, Romania.

1299

We investigated some bio- and histochemical parameters, less studied in experimental rickets, i.e. urinary elimination of hydroxiproline and in the bones alkaline phosphatase (chemically and histochemically) and tissue respiration by the Warburg method. Studies were performed on two groups of white Wistar rats. The first group had been on a normal diet for our breeding stock. The second group was fed a rachitogenic diet with some modifications according to the 3241 McCollum diet. The animals, 30 days old at the beginning of the experiments, were followed during 1 month then sacrificed by decapitation. The clinical modifications (appearance weight and length and the radiologic aspect of the bones, blood Ca, P and alkaline phosphatase, the histologic appearance of the tibia were all consistent with data reported in the literature. Urine hydroxiproline assays showed a more reduced elimination in the rickety than in the normal animals. The chemical and histochemical evaluation of alkaline phosphatase, as well as respiration in bone tissue, differed from the normal values.

THE ROLE OF NON SPECIFIC AFFERENTATION IN THE REGULATION OF BREATHING.

F.Paleček, M.Chválová. Inst.of Pathophysiology, Faculty of Pediatrics,
Charles University, Prague, Czechoslovakia.

We attempted to quantify the role of non specific afferentation in rats. We used the method of carbon dioxide ventilatory response curves. These were constructed in rats in electroanesthesia and in urethane anesthetized rats; the latter were intact or myelotomized or electrically stimulated (the sciatic nerve). A) There was a parallel shift of the CO2 response curves, dependent on the level of non specific afferentation. B) Short-lasting electrical stimulation of the central stump of the sciatic nerve in vagotomized rats had an effect similar to vagus stimulation: when applied during inspiration, it reversed the phase of the cycle; it prolonged the expiratory phase when applied during expiration. It is concluded that: 1. Non specific afferentation participates in a decisive way on the responsivity of central regulatory mechanisms to CO2; 2. Powerful stimuli along the non specific afferents can override the lack of specific (vagus) afferentation.

1301 DELAYED REGENERATION OF CENTRAL SYNAPSES BY INSECT SENSORY CELLS. J. Palka and J. S. Edwards, Dept. of Zoology, Univ. of Washington, Seattle, Washington 98105, USA.

The paired abdominal cerci of crickets regenerate when removed in an immature individual. Regeneration can be delayed for any desired number of instars by repeated removal of initial rudiments, which lack sensilla. Since the somata of insect sensory cells are peripheral, not central as in vertebrate systems, the sensory neurons which differentiate within the epidermis of regenerate cerci are a completely new cell population. They send axons to the terminal ganglion of the c.n.s., where they form new functional connections with giant interneurons. Testing the responses of physiologically identified interneurons to controlled stimuli reveals no significant differences between normal animals and bilateral regenerates, even when cerci are removed at hatching and prevented from regenerating up to the 7th of the 9 larval instars. Cercal axons are the major, if not the sole input to the giant interneurons. Yet their prolonged absence has no significant effect on the cytological appearance of the somata or the diameter of the axons of the interneurons, or on their ability to establish correct connections with sensory neurons newly differentiated in the periphery. The only instances thus far identified of "wrong" central synapses are contralateral connections in a normally ipsilateral pathway, formed in animals raised with a single, unpaired cercus. This consistent formation of input not only to the correct ipsilateral interneurons but also to their contralateral homologues contributes to the study of factors maintaining ipsilaterality during normal development.

1302 ELECTROPHYSIOLOGICAL ANALYSIS OF A COMPOUND SENSE ORGAN, THE PECTINE OF THE SCORPION. K.Pampapathi Rao. Dept. of Zoology, Bangalore University, Bangalore-1, India.

Pectines are unique to scorpions. The number of teeth on the comblike organ is variable and bears a relationship to the ecophysiological situation of the occurrence of the different groups of scorpions. On each of the teeth, there occurs a specialized area on the ventral side containing a large number of short basiconic pegs, which are permeable at their tips to salt solutions. At the base of each pectinal tooth are a cluster of short, stiff hairs and distributed elsewhere on the pectines are relatively long hairs. Recordings from the pectinal nerve responses were obtained from the different hairs. Mechanical stimuli alone elicited phasic bursts of impulses from the stiff short hairs and the long hairs. This mode of recording did not yield clear cut responses from the basiconic pegs of the specialized sensory areas. Recording with glass capillary electrodes (a la Hodgson) excellent responses were obtained from these sensory pegs, indicating the chemoreceptive nature of these structures. A detailed analysis of the sensitivity of these pegs to different salts, sugars and aminoacids has been made. The other types of hairs on the pectines are not chemoreceptive.

MITOCHONDRIAL AND MICROSOMAL PHOSPHOLIPID CLASSES IN MYOCARDIAL TISSUE FROM FAILING RAT HEART-LUNG PREPARATION (HLP).

V. Panagia and R. Minelli. Inst. of Human Physiology - Univ. of Pavia, PAVIA (ITALY)

Because previous results had shown that experimental heart failure was not caused by

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reduction of oxydable substrate (glycogen, neutral lipids) and high-energy phosphate content in myocardial tissue, present experiments have been performed in order to see if any alteration in subcellular membranes, which are strictly involved in excitation-contraction coupling mechanism, could be detected in failing heart. Experimental cardiac failure was realized by imposing high power level on left ventricle of rat's HLP. The evaluation of mitochondrial and microsomal phospholipid classes have shown: 1) no change in mitochondrial phospholipids and 2) a 20% reduction in phosphatidylcholine, 35% in phosphatidylserine and 34% in sphingomyelin in microsomal fraction from failed heart. These biochemical changes could also elucidate the impaired functional activity of sarcoplasmic reticulum from failing heart observed "in vitro" by several Authors.

TEMPERATURE AND CALCIUM SENSIBILITY OF SLOW POTENTIALS FROM SMOOTH MUSCLES OF THE CAT'S STOMACH. M. Papasova, K. Boev, J. Lucanov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

1304

Studies were made of the changes in the pattern of slow potentials (SP) recorded by the pressure electrode from the smooth muscle of the cat's stomach (in vitro experiments). Changes in the temperature of the Tyrode solution led to considerable changes in the frequency, amplitude and velocity of conduction of SP. In the temperature interval from 30 to 15°C the SP duration was found to be prolonged as a result of the correspondent increase in the duration of the different phases of SP. The increase in the Ca⁺⁺ concentration (from 1.7 to 2.125 mM, 2.55 mM, 2.975 mM to 3.4 mM) provoked an increase in the frequency of SP, shortened the duration of the second component of SP and affected considerably the velocity of conduction. The SP frequency increased by raising the temperature and remained constant in the temperature interval from 33 to 37°C. Maximum velocity of conduction was found at 35 to 37°C. Increasing the Ca⁺⁺ concentration led to a considerable increase in the SP frequency in the above mentioned temperature interval as in the case of Ca⁺⁺ concentration above 2.975 mM the changes were linear.

INDUCTION OF SLOW WAVE SLEEP BY A FACTOR RELEASED INTO CEREBROSPINAL FLUID (CSF) DURING SLEEP DEPRIVATION. J.R. Pappenheimer, G. Koski and V. Fencl. Dep. of Physiology, Harvard Medical School, Boston, Mass., U.S.A.

1305

Rats with chronically implanted ventricular guide tubes and EEG electrodes were maintained in activity cages on a 12 hour alternating cycle of light and darkness. Intraventricular infusion of a low molecular weight fraction of CSF from sleep-deprived goats (0.2 ml in 1 hour, just prior to the dark cycle) prolongs slow wave sleep time and depresses locomotor activity by 40-50% during the subsequent 6 hours. The effects are significantly greater than those which follow infusion of control fluids. Subarachnoid infusions are ineffective. Concentration of the sleep-promoting Factor S increases progressively in CSF of goats during the first 48 hours of sleep deprivation. Factor S has a M.W.<500; its effects cannot be simulated by intraventricular infusions of serotonin, GABA, glutamate, 4-OH butyrate or butyrolactone in physiological concentrations. Properties of Factor S suggest that it may play a role in normal regulation of sleep and wakefulness.

TRANSIENT CONDUCTANCE CHANGES INDUCED BY PRESSURE IN ARTIFICIAL LIPIDIC MEMBRANES.

M. Parisi. Instituto de Anatomia General y Embriologia, Faculty of Medicine, University of Buenos Aires, Buenos Aires, Argentina.

Hydrostatic pressure, applied to one side of artificial lipidic (i.e. black) membranes made by the method of Mueller,Rudin,Tien and Wescott, modifies their electrical properties. A reversible potential function of order three was founded between the applied pressure and the increase in conductance and at a given "threshold" value the stimulus produces a transient change in the conductance of the membrane, followed by a "refractive period". These effects are strongly dependent on calcium concentration and on the origin of the membrane lipidic compounds. The studies were carried out on lipidic membranes made with phospholipids of ox brain gray matter or from toad urinary bladder in a solution of chloroform-methanol-tetradecane with the addition of pure cholesterol. The mean measured membrane resistence was $4.2 \pm 0.6 \times 10^5$ ohm cm²(n=10). Some type of mechano-electrical transductions seems to be the key feature in the physiological response of different biological structures such as the baroceptors, the Pacinian corpuscle, stretch muscle receptors, etc. Our results show that a relative simple lipidic membrane can modify its structure in a dinamic way producting electrical changes that may be related to those described in biological membranes. The important role of lipidic composition on permeability phenomena is emphasized by the transient response here described in "protein-free" membranes.

1307 SLEEP RELATED CHANGES IN HYPOTHALAMIC UNIT ACTIVITY AND SPECIFIC THERMAL RESPONSES. P.L. Parmeggiani, C. Franzini and P. Lenzi. Istituto di Fisiologia umana, II Cattedra, Università di Bologna, Bologna, Italia.

Unanaesthetized unrestrained cats were exposed to constant environmental temperatures ranging from -15 to 35°C. a) At all temperatures anterior and dorsal hypothalamic areas unit activity decreases in late slow-wave sleep (SWS) and is tonically depressed in fast-wave sleep (FWS); lateral hypothalamic area unit activity increases in FWS; some units of lateral hypothalamic area tuberal division are less active in FWS than in SWS; fields of Forel and zona incerta unit activity also increases in FWS. These changes are independent of hypothalamic temperature increase in FWS. b) At temperatures eliciting shivering or panting these specific thermal responses disappear only in coincidence with FWS. c) The slopes of subcutaneous body temperature changes during SWS and FWS are negatively and positively correlated, respectively, to environmental temperature. The observed phenomena suggest that an alteration in hypothalamic control of homeostasis, during FWS, underlies the change from homoiothermic to poikilothermic regulation.

MORPHOLOGICAL CLASSIFICATION OF THE HORIZONTAL CELLS IN THE TELEOST RETINA. V. Parthe. Dept. Neurobiology. IVIC, Caracas, Venezuela.

In disagreement with what is known, it is demonstrated by means of the Golgi method the existence of two classes of horizontal cells in the teleost retina: 1) the external, medial and internal horizontals (Cajals' terminology), which are organized in three layers of cells, the ascending processes of which terminate in contact with the cone pedicles. Only in the external horizontal a lateral expansion was observed, which seems to represent a short axon, but its termination is still unknown; and 2) a new species of horizontal cell organized in a single layer of cells, the ascending processes of which terminate in form of branchlets at the level of the rod spherules. On the basis of the connections with the receptors, the horizontal cells should be classified as: 1) CONE HORIZONTAL CELLS subdivided in EXTERNAL, MEDIAL and INTERNAL ones, which are in contact with cones only; and 2) ROD HORIZONTAL CELLS which consist of one type of cells which make synaptic contact exclusively with rods. The above classification agrees with marking experiments (Svaetichin, Negishi and Parthe, 1969, 1971), which demonstrated the origins of photopic L-type S-potentials in external, of C-type S-potentials in medial and internal horizontal cells respectively, and of scotopic L-type S-potential in the rod horizontal cells.

FACTORS IN MECHANICAL COMPLIANCE IN THE MOTOR SYSTEM. Lloyd D. Partridge and Henri Demieville. Department of Physiology & Biophysics, University of Tennessee Medical Units, Memphis, Tennessee, USA.

1309

Models of parts of the motor system have been constructed using physiological muscles but replacing some of the neural elements by hardware components. In these models it is possible to analyze interacting factors more easily than in the intact physiological system. One form for representing the interactions describes the stiffness of an individual motor unit in terms of: a passive stiffness, a stiffness from the effect of tonic excitation, and an additional stiffness—like factor resulting from reflex changes in excitation. The overall stiffness as observed with passive stretches involves the sum of all of these components. A similar division into passive, tonic, and reflex terms can be made for viscosity—like effects. The properties of each of these three types of contribution to compliance differ. When a muscle is made up of multiple interacting motor units the overall response to stretch involves interactions between the individual units and can not be looked upon as a simple sum of the independent responses.

EFFECT OF EXPERIMENTAL HYPOTHYROIDISM ON SYNAPTIC TRANSMISSION IN CAT SYMPATHETIC AUTONOMIC GANGLIA. <u>Lidia Pascalov-Stoenescu</u> and <u>Nicolae Sterescu</u>. "D. Danielopolu" Inst. of Physiology, Academy of Medical Sciences, Bucharest, Romania.

1310

Work was performed in 40 cats,17 with experimental hypothyroidism induced by chronic administration of methyltiouracil.Postganglionic potentials in the inferior mesenteric ganglion in situ were recorded using the post-tetanic potentiation phenomenon (PTP) as an index for the functional state of presynaptic terminals.Post-ganglionic potentials were recorded prior to repetitive stimulation, then lo,20 and 30 sec after interruption of excitation and every 30 sec until complete extinction of the phenomenon. The results showed that while the amplitude and pattern of post-ganglionic potential do not differ in either group; PTP presents a clear-cut modification.PTP amplitude was reduced in the experimental group, the maximum value calculated on the arithmetic mean curve being of 124±3% as compared with 146±7% in controls, a highly significant decrease (p<.ool). PTP amplitude fell gradually in experimental group and occasionally completely disappeared within 25-30 min from the beginning of the experiment, whereas in controls PTP values were constant for 2 to 3 hrs.

1311

EFFECT OF CO₂ ON LOCAL BLOOD FLOW IN VARIOUS PARTS OF THE BRAIN.

E.Pásztor, P.Sándor, A.G.B.Kovách. Inst. of Neurosurgery and Experimental Research Department of Semmelweis Medical University, Budapest, Hungary:

Local blood flow was determined in 29 dogs under chloralose anesthesia using the hydrogen clearance method. The following mean values were found: parietal cortex = 48 ml/loo g.min, n=65; subcortical white matter = 16 ml/loo g.min, n=43; and thalamic VPL nucleus = 35 ml/loo g.min, n = 45. Following CO2 inhalation, the arterial pCO2 increased from 38 mm Hg to 56 mm Hg, the mean arterial blood pressure slightly decreased. Blood pH decreased from 7.22 to 7.12. The Hb O2 saturation of 93% remained unchanged. CO2 inhalation increased the local blood flow by 31% in the cortex, 52% in the white matter and 64% in the thalamus. Simultaneous measurements on the three area in the same animal presented similar results /in the cortex 21%, in the white matter 41% and in the thalamus 72% increase/. Thus, quantitative differences were found among the various parts of the brain concerning the response of blood flow to CO2 inhalation.

1312 INHIBITION OF SPONTANEOUS CONTRACTILITY OF RABBIT DETRUSOR MUSCLE PRODUCED BY NA PUMPING.

David M. Paton. Dept. of Pharmacology, Univ. of Alberta, Edmonton 7, Alberta, Canada.

The effects of Na⁺ pumping on spontaneous isometric contractions of rabbit detrusor muscle strips have been studied in partially Na⁺-rich tissues. Addition of as little as 1.5 mM K⁺ to strips in K⁺-free Krebs medium at 37°C produced immediate inhibition of spontaneous contractility and relaxation, the duration of these effects being directly related to the duration of previous K⁺ omission. The addition of Rb⁺ and Cs⁺ but not of Li⁺ had similar effects on contractility, the order of potency being K⁺=Rb⁺>Cs⁺>>Li⁺. These K⁺-induced changes in contractility were prevented by ouabain in concentrations which inhibited Na⁺ pumping in this tissue, but were not altered by reduction of Cl⁻ in the medium to 3 mM or by drug antagonists. The addition of 30-45 mM K⁺ to tissues in K⁺-free medium produced temporary inhibition of contractility whereas similar additions to tissues in Krebs medium containing 4.6 mM K⁺ produced immediate large contractions. The removal of K⁺ or the addition of ouabain to tissues whose contractility was inhibited by K⁺, resulted in the rapid restoration of spontaneous contractility. These findings suggest that the addition of K⁺ to tissues in K⁺-free medium activated electrogenic Na⁺ pumping resulting in membrane hyperpolarisation and inhibition of contractility. The removal of K⁺ may have produced inhibition of such pumping causing depolarisation and restoration of spontaneous contractility. (Supported by a grant from the Alberta Heart Foundation).

1313 IN VIVO MEASUREMENT OF VENTRICULAR & AORTIC DIMENSIONS USING F.M. AND PULSED ULTRASOUND.

T.Patrick, W.Kemper, S.Vatner, C.Higgins, D. Franklin. Scripps Clinic & Res. Fndn., and UCSD Med. Sch., La Jolla, Cal., U.S.A.

Studies of the mechanical properties of heart muscle and aorta are important in further understanding of cardiovascular dynamics. We have developed techniques using frequency modulated (F.M.) and pulsed ultrasound which offer direct measurement of organ dimensions (L.ventricle and aorta) in intact, unanesthetized animals. The first technique measures the transit time of a continuous F.M. acoustic signal propagated between two piezoelectric crystals. The resulting difference frequency between transmitted and received signals is proportional to crystal separation, and rate-of-change of frequency. This device features small size, low power consumption, its output is suitable for direct telemetry from free-ranging animals, and is compatible with F.M. flow instrumentation. The second technique measures the transit time of acoustic pulses (1kHz rate) propagated between the two crystals. This device is compact (9 X6.5 X 11 cm including batteries), is useable in a synchronous mode with a pulsed electromagnatic blood flowmeter and has a minimum measurement range of 5 mm. The unit is routinely used as part of a system for measurement of L.V. dimensions and rate-of-change of dimensions, along with L.V. pressure and dp/dt to define changes in the contractile state of the myocardium in normal conscious animals.

1314 CLIMBING FIBRE INPUT TO CAT CEREBELLUM. D.H. Paul, M. Gresty & Ann Latham. Dept. of Physiology, Manchester University, Manchester M13 9PL, U.K.

Purkinje cells (PC) have been activated via their climbing fibre (CF) afferents following stimulation of peripheral nerves (superficial radial, dorsal cutaneous branch of peroneal), regions of the CNS (caudate mucl., pons, substantia nigra) and cerebellar white matter. Spontaneous CF responses have also been recorded. The consequences of CF activation of a PC are (1) a brief excitation lasting up to 15 msec and producing a burst of spikes at about 500 Hz; (2) a variable period of 30-100 or more msec during which a second extracerebellar stimulus fails to evoke a second CF response. White matter stimulation is still effective during this time. In addition, many cells show a period of suppression of spontaneous activity following a CF response. These results suggest that control of impulse traffic along CF paths is regulated at a subcerebellar level, whilst the arrival of CF impulses at the cerebellar cortex triggers a mechanism which may lead to the suppression of spontaneous PC activity. Responses of fastigial nucleus neurones show periods of high frequency discharge following stimulation of peripheral nerves or the CNS sites with single shocks. These responses have been interpreted as due to disinhibition of the nuclear cells during periods when the spontaneous activity of PCs has been suppressed following a CF activation.

CARDIO-VENTILATORY RESPONSES TO ELECTRICAL STIMULATION OF THE FEMORAL NERVE IN MAN. P.-E. Paulev and D.M. Cicak, Inst. of Medical Physiology B, University of Copenhagen, Copenhagen, Denmark.

1315

Painless stimulation of the femoral nerve using surface electrodes can produce a vigorous contraction of the quadriceps femoralis muscle. In order to compare the cardio-ventilatory responses to a peripherally induced muscular contraction with those elicited by a voluntary contraction (kick), such stimulations were used on relaxed, seated subjects, who were protected audio-visually, and had become well accustomed to the procedure. In response to a voluntary kick, heart rate (instantaneous cardiotachograph) rose 9% at the 3rd beat, and maximal ventilatory volume rate, dVmax/dt (pneumotachograph), increased 14% in the first subsequent breath. In response to electrical stimulation induced by the experimenter, however, the same variables showed a 17% and 29% rise, respectively. In a series where the subjects effected the stimulus by pressing the button themselves, the cardiac response was identical to that after a voluntary kick, but no significant change was observed in dVmax/dt of the first breath. A startle effect was concluded to be operating in the experimenter-induced-stimulus series, but the self-induced series, where no surprise factor was present, suggests a local mechanism in the limbs transmitting neural information to trigger the initial rise in heart rate, but no immediate ventilatory responses.

1316

DISSOCIATION BETWEEN THE HEART RATE AND THE CONDUCTION TIME DURING VAGAL STIMULATION. V.Pavlov, S.Mileva, G.Spassov. Inst.of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Evidence is presented to show that during vagal efferent stimulation in cats, the decrease of the heart rate and the prolongation of the conduction time do not develop simultaneously. In the majority of the cases (above 50%) the conduction from the atria to the ventricles is first delayed and later, just before the end of stimulation, it begins improving. At the same time, the bradycardia is intensifying continuously. This phenomenon, marked as dissociation between the heart rate and the conduction time, prevents the development of the atrioventricular block. Dissociation occurs when the bradycardia reaches a determined level. When the decrease of the heart rate is poorly expressed, the conduction time increases continuously during the stimulation and terminates ordinarilly with a block.

1317

MARKING EXTRAOCULAR MUSCLE FIBERS FOR PHYSIOLOGICAL-MORPHOLOGICAL CORRELATION. Lee D. Peachey, Carol Hudson and Paul Bach-y-Rita, Biology Dept., Univ. of Penna., Philadelphia, Penna. and Inst. Visual Sciences, Pacific Medical Center, San Francisco, Calif., U.S.A.

Mammalian extraocular muscles contain at least five muscle fiber types distinguishable physiologically and morphologically. Using Fast Green FCF or Methyl Blue dye methods for marking fibers after intracellular recording, we have had trouble with fading of the dye spots, and have found a procion dye to give better results. Microelectrodes filled with ~3% Procion Rubine MB (Imperial Chemical Industries) and ~3% HCHO, and having resistances of 50-100 M were used for intracellular recording from muscle fibers of in situ superior rectus muscles of anesthetized cats. After recording, a current of ~ 2ua. was passed (electrode negative) for ~15 sec., leaving a spot of red dye in the fiber. Several fibers could be labelled in each muscle. The muscles were fixed in situ with HCHO and then removed from the cat. Bundles of fibers, each including one spot, were dissected and processed for electron microscopy by conventional methods using osmium tetroxide and epoxy resin. The dye spots remained distinct before and after fixation and in the final embeddings, and could be used to identify fibers recorded from. Thick (2µ) sections were used to locate labelled fibers in the light microscope. Thinner sections were used for electron microscopy of the same fibers. Damage near the site of labelling was often severe, but serial transverse sections traced the labelled fiber away from the damaged region to a region where preservation was good. (NSF GB-6975x)

1318 LOCATION OF RECEPTORS FOR SALT GLAND SECRETION IN THE GOOSE. M. Peaker, Ann Hanwell & J.L. Linzell. ARC Inst. Animal Physiology, Babraham, Cambridge, U.K.

> Schmidt-Nielsen thought that the receptors responsible for detecting a salt load and initiating salt gland secretion in marine birds lie in the CNS. We have evidence that they lie in the heart. Osmo-receptors and not volume receptors appear to be responsible since as well as NaCl, Na SO, LiCl and sucrose initiate secretion and increase heart rate when infused into the right atrium whereas large volumes of homologous blood have no effect. Hypertonic NaCl infused into the carotid arteries, hepatic or renal portal veins did not induce secretion. Section or local anaesthesia of the vagi in the neck prevented or abolished secretion but below the heart had no effect. Stimulation of the vagi in a decerebrate bird initiated secretion. Local anaesthetic injected with methylene blue into the pericardial sac abolished secretion with the same time course as vagal block; the base of the heart was most heavily stained. We conclude that osmo-receptors, probably situated in the right or possibly left atrium, initiate salt gland secretion.

SENSITIZATION OF FLEXOR-WITHDRAWAL REFLEX IN CONSCIOUS SPINAL RATS. 1319 J.A.Pearson. Dept.of Physiology, University of British Columbia, Vancouver British-Columbia, Canada.

Repeated elicitation of the flexor reflex in anaesthetized spinal cats can result in incremental changes in response (sensitization). This is in contrast with findings in conscious spinal animals in which only decremental changes (habituation) were observed. This study reinvestigated these ap-

parently contradictory observations.

Conscious rats were tested 1, 3 or 5 days after spinal transection at the 11th thoracic vertebra. Integrated EMG activity recorded from the biceps femoris muscle was used as an index of flexor reflex activity. Electrical stimuli were applied to the ipsilateral hind paw with inter-stimulus intervals of 1 or 10 secs. Reflex responses following repeated stimuli showed significant increases over initial responses. Degree of sensitization was related neither to time allowed for recovery from transection, nor to the interstimulus interval. Identical experiments in rats with intact spinal cords showed a progressive decrement in the flexor reflex response.

Experiments described here demonstrate not only a failure of the spinal animal to habituate, but show a phenomenon of response increment, the mechanism of which is not as yet understood.

SYNAPTIC TRANSMISSION IN THE DEGENERATING LATERAL GENICULATE NUCLEUS, EL--1320 ECTROPHYSIOLOGY AND ULTRASTRUCTURE. J. Pecci Saavedra, O.L. Vaccarezza, T. A. Reader and E. Pasqualini. Inst. of Gen. Anat. and Embriol., School of

Medicine, Univ. of Buenos Aires, Argentina.

The ultrastructural and electrophysiological alterations taking place in the lateral geniculate nucleus of cats were studied in two conditions: a) after bilateral eye enucleation; and b) after electrolytic or surgical section of the optic tract. In both cases, a progressive decrease in the number of synaptic vesicles and increase of neurofilaments was found in the retinal synapses of the nucleus. In (a) the "dark degeneration" stage was reached in 120 hs while in (b) in 72 hs. Synaptic transmission ceased at 72-96 hs in (a) and at 48-54 hs in (b). The recovery cycle of the generation is a synapse of the generation of vertical contents. niculate cells showed a progressive deterioration of responsiveness. The results are interpreted as due to a decrease in the amount of available transmitter for release and to alterations in transmitter synthesis. The differential temporal course of the alterations in conditions (a) and (b) is related to the corresponding lengths of the remaining axon stump. In (a) that length is about 35 mm, while in (b) it is about 7 mm.

1321

A NON-LINEAR THEORY OF THE DISTRIBUTION OF PULMONARY VENTILATION
T.J. Pedley, N.F. Sudlow, J. Milic-Emili: P.F.S.U. Imperial College, London.

The theory for the distribution of ventilation between the upper and lower lobes of a two compartment model of the lung is developed, neglecting inertia, but allowing resistance and compliance to vary with lung volume and resistance to vary with flow rate, all in a nonlinear manner. The results show how a bolus of labelled gas inspired at various volumes and flow rates would be distributed. The bolus is distributed preferentially to the lower lobes if inspired slowly because they are more compliant than the upper as a result of the gradient of pleural pressure. Jith increasing inspiratory flow rate more of the inspired bolus is distributed to the upper lobes. 'Cross-over', where ventilation per alveolus in the upper and lower lobes is equal after a given inspired volume, occurs at approximately 2 litres/sec. when the inspired volume is 400 ml. Above this flow rate there is a preferential distribution of gas to the upper lobes. Cross-over is a direct result of the volume-dependence of resistance, the more expanded upper airways having a lower resistance. The flow rate at which 'cross-over' occurs is influenced to some extent by all parameters of the model (e.g. overall airway resistance, shape of the pressure-volume curve), but is most sensitive to changes in the lung volume at which the bolus of gas is injected, The results are in good agreement with recent experiments on the distribution of boluses of radioactive Xenon. The theory can readily be extended to calculate the distribution of ventilation in situation other than uniform inspiration.

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INTESTINAL METABOLISM AND TRANSPORT OF A PESTICIDAL CARBAMATE IN-VITRO. J. C. Pekas. USDA, ARS, Metabolism and Radiation Research Laboratory, Fargo, N. D., USA.

(1-Naphthyl-1-1⁴C) N-methylcarbamate (*NC), an insecticide, was incorporated into media (10⁻⁵ M) of everted sacs of rat small intestine. A pH 6.5 medium was used because *NC decomposed during incubation in pH 7.4 medium (20%/2 hr). ¹⁴C-naphthol (*N) was liberated from *NC in the presence of everted sacs, demonstrating enzymic hydrolysis of *NC. The liberated *N was conjugated to form ¹⁴C-naphthyl glucuronide (*NG). Both of these reactions were more rapid in sacs of cranial than of caudal intestine. Net transfer of ¹⁴C from mucosal to serosal fluid was demonstrated with all intestinal sacs; however, the quantity (µmole) of net transfer decreased from cranial to caudal intestine. The quantity of net transfer of ¹⁴C was associated with the quantity of water-soluble ¹⁴C-metabolites in serosal fluid (primarily *NG). The concentration of total ¹⁴C and of ¹⁴C-metabolites after incubation was always higher in serosal than in mucosal fluid. Similar experiments were conducted in which *N was substituted for *NC on an equimolar basis. The rates of *NG synthesis and ¹⁴C-label transfer to serosal fluid were nearly 10 times that obtained with *NC. *NG was the major ¹⁴C-component (99%) in serosal fluid. Anaerobiosis reduced the quantity of *NG synthesized and eliminated net transfer to serosal fluid with both *NC and *N substrates. A Na-free medium suppressed both the quantity of *NG synthesized and net transfer.

1323

MODE OF ACTION OF RYANODINE ON HEART MUSCLE. Zia J. Penefsky, Dept. of Physiology, Mt. Sinai School of Medicine, of the City University of New York, N. Y., U.S.A.

The alkaloid ryanodine exerts a negative inotropic effect on cardiac muscle. In order to investigate the possibility that this effect of ryanodine is a result of interference with the regulation of Ca^{++} release by the sarcoplasmic reticulum system (SR), advantage has been taken of the fact that the SR, as visualized in the electron microscope, is undeveloped in the fetal mammalian heart and poorly developed in toad heart. Ryanodine (1.5 to 3.5 X 10^{-6} M) caused 50 to 80% inhibition of contractile tension in adult mammalian cardiac muscle but was without effect on fetal cardiac muscle from the same species or on the toad heart. The conclusion that ryanodine blocks the delivery of Ca^{++} by the SR is supported by the following findings: (1) inhibition by ryanodine is reversed by high Ca^{+-} concentrations in the bathing medium ($[Ca^{++}]_0$) but reappears at normal $[Ca^{++}]_0$ (Am. J. Physiol. 218, 1682, 1970); (2) ryanodine appears to exert little or no effect on cardiac muscle (fetal mammalian and toad) which are deficient in SR; and (3) the development of contractile tension by toad and fetal mammalian cardiac muscle was more dependent on $[Ca^{++}]_0$ than adult mammalian cardiac muscle.

CIRCANNUAL RHYTHMICITY IN HIBERNATING GROUND SQUIRRELS, CITELLUS LATERALIS, IN RELATION TO SEX AND OPPORTUNITY TO BREED. E. T. Pengelley and Sally J. Asmundson. Dept. of Life Sciences, Univ. of California, Riverside, Calif., 92502., U.S.A.

The annual homothermic-heterothermic and body weight cycles of 20 adult males and 20 adult females trapped in August and placed under constant conditions of a 12 hour photoperiod and 3°C temperature on Oct. 1 were studied. The same cycles were studied in 20 females trapped in May, 10 of which were pregnant and successfully raised their litters and 10 of which were not pregnant. These females were kept on a 12 hour photoperiod at 23°C until August 1 and were then transferred to a 3°C room with a 12 Hour photoperiod. All animals were individually caged with ample bedding and food and water ad libitum. Initial results indicate 1) that females who do not breed in the spring fatten and enter hibernation earlier than females who breed and raise a litter, 2) females whether or not they have raised a litter enter hibernation earlier and spend more days in hibernation than males, and 3) males show more aberant hibernation patterns including no hibernation more than do females. Implications are that for females at least, the opportunity to breed successfully is a factor in the synchronization of the animals temporal physiology to the environment. These experiments will be continued for as long as possible to determine if these differences will persist over periods of several years when the animals are kept under constant environmental conditions. Supported by Grant GB8605 from National Science Foundation.

1325 COMPARISON BETWEEN THE IMMEDIATE EFFECTS OF ELASTIC AND FLOW RESISTIVE LOADS TO BREATHING IN CATS. L.D. Pengelly, H. Strobach, and S. Iscoe. Physiology Dept., McGill Univ., Montreal, Canada.

The first-breath response to flow-resistive as well as elastic inspiratory loads was studied in cats anaesthetized with nembutal. Measurements were made of tracheal pressure, airflow, and lung volume, in a body plethysmograph. Experiments were performed both during quiet breathing, and during ventilation increased by inhaled $\rm CO_2$ mixtures before and following bilateral cervical vagotomy. Tidal volume ($\rm V_T$) fell progressively with increasing loads, both flow-resistive and elastic. Tracheal pressure became progressively more subatmospheric for increasing resistive loads; especially between 0.5 and 0.7 $\rm V_T$ control, where maximum flow occurred. Maximum flow was reduced progressively from control values. End-inspiratory tracheal pressure also became more subatmospheric for increasing elastic loads. Adding an elastic load equivalent to ten times the passive respiratory system gave a loaded tidal volume of approximately 0.5 $\rm V_T$ before; and 0.3 $\rm V_T$ after vagotomy. Adding a resistive load equivalent to ten times the passive respiratory system gave a loaded tidal volume of approximately 0.8 $\rm V_T$ before; and 0.7 $\rm V_T$ after vagotomy. These data indicate that elastic loads produce a more severe reduction in tidal volume of the respiratory system than resistive loads of the same magnitude.

Supported by the Medical Research Council of Quebec.

1326 GASTRIC MUCOSAL HISTAMINE DURING HYDROCHLORIC ACID SECRETION IN ANAESTHETIZED DOGS. H.G. PERCIVAL. Sherrington Sch. of Physiology, St. Thomas's Hosp. Med. Sch., London S.E. 1, England.

The aim was to investigate the mucosal histamine content of secreting gastric mucosal in anaesthetized greyhounds at different times during the application of a pentagastrin infusion stimulus(0.1µg/kg/min). It was intended to demonstrate a fall in mucosal histamine content due to histamine liberation associated with the onset of gastric acid secretion in dogs, similar to that reported in rats. Greyhounds were operated on under pentobarbitone anaesthesia (30mg/kg IV initially) through midline abdominal incisions. Their spleens were removed, pyloruses tied and a gastric cannula was implanted approximately 15cm from the pylorus close to the greater curvature. Collections of gastric acid from whole stomachs were made with dogs lying in the left lateral position. Samples of gastric mucosa were obtained from the gastric bodies by a method recently demonstrated (Percival, 1971). The mucosal samples obtained were assayed for histamine content using a guineapig ileum preparation. The results showed no significant fall in the mucosal histamine content during the initial 90min. period of acid secretion. Studies made over longer periods (2,4,6& 8hrs) also show no mucosal histamine depletion of secreting gastric mucosa. It was concluded that the mechanism of acid secretion may differ in dogs from that in rats. Therefore the direct relevance to man of the feedback mechanism demonstrated by experiments in rats is questioned.

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THE INFLUENCE OF THE INTRAOCULAR BLOOD CONTENT ON THE RELATIVE SPECTRAL SENSITIVITY IN ALBINO RABBIT. J.Peregrin. Dept.of Physiology, Charles University Med. Faculty, Hradec Králové, CSSR.

After traversing the retina and the choroid, the incident light is diffusely reflected back by the scleral inner surface. In the spectral regions, where the absorbance of receptor pigments and of hemoglobin is low, the amount of the diffusely reflected light is almost equal to the amount of the incident light. Thus, in albino animals, in these spectral regions the total amount of light which excites the receptors is nearly doubled in comparison with the pigmented animals. This finding constitutes a basis for the configurational changes of the relative spectral sensitivity curves, which, without appropriate corrections, may lead to false interpretations. The evidence of the influence of blood layers of various thicknesses in transpupillary and diascleral illumination on relative spectral sensitivity curves in albino- and pigmented animals is presented.

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A CONTRIBUTION TO THE KNOWLEDGE OF THE ROLE OF THE FLEECE IN THERMOREGULATION IN TROPICAL ENVIRONMENT. N. Pereira and E. Gonzalez-Jimenez, Inst. de Produccion Animal, Facultad de Agronomia - U.C.V., Maracay, Venezuela.

To study the role of the fleece in thermoregulation an experiment was designed and conducted with sheep grazing in the tropical plains of Venezuela. Twelve mature male Merino sheep were divided into two groups, clipped and fully fleeced. The animals were studied during three two weeks experimental period while grazing in open country. The change in heat storage was computed from measurements of rectal, skin and fleece temperatures. The heat storage was greater in shorn sheep. This result suggests that in tropical environment the fleece reduce the gain of heat from the surrounding.

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ACETYLCHOLINE MEDIATION OF HABITUATED WITHDRAWAL RESPONSES IN APLYSIA GILL. B. Penetz, G. I. Roth, and J. Estes. Univ. of Kentucky Med. Ctr., Lexington, Ky. 40506, USA.

Habituation has been shown in Aplysia gill after removal of CNS; neural organization in the gill appears responsible for habituation; the habituated behavior is a withdrawal movement of one gill lobe (pinnule) in response to water drops falling on it (Peretz, 1970). Rate of habituation is hastened by about 50% when gill is continuously infused with acetylcholine (ACH), 50 µg/ml, contrasted to infusion of sea water or no infusion. Dishabituation is elicited, as in controls, by electrical stimulation of pinnule and nerve trunks innervating gill. Spontaneous recovery of the behavior is also seen. Infused Physostigmine appears to give similar results to ACH. Histochemistry of the gill shows acetylcholinesterase present along nerve fibers. ACH, presumably accumulating in the gill neural plexus, is suggested as one neurotransmitter mediating habituation.

(NIMH-MH18611, UKGRSG- 5-S01-FR05314)

1330 ELECTROPHYSIOLOGY OF CONTRA-AND IPSILATERAL VISUAL PROJECTIONS TO THE WULST IN PIGEON. M. Perisic, J. Mihailovic, M. Cuénod., Brain Res. Inst., Zurich, Switzerland.

Despite total crossing of the optic nerve (NO) fibres in the chiasm bilateral visual information is available to the telencephalon of the pigeon by ways of interhemispheric commissural systems. The supraoptic decussation (DSO) appears to be important. The retino-thalamo-hyperstriatal (wulst) pathway has been studied in 64 animals by means of evoked potential and single unit recordings. Potentials evoked by electrical and photical (diffuse light) stimulation of either eye were recorded in both contra- and ipsilateral wulst. Electrolytical lesion or revesible cooling of the rostral part of the DSO strongly diminished ipsilaterally evoked responses, whereas contralateral ones remained unaffected. Among 125 wulst units 52% were activated solely by contralateral NO stimulation, these were located dorsally; 25% were activated exclusively ipsilaterally and were located ventrally, while 23% were activated bilaterally and had an intermediate wulst location. The response evoked in both wulsts by stimulating one eye was strongly diminished by cooling the contralateral dorsolateral thalamus (DL). Thus, DL appears to be a relay in the visual projection pathway to the forebrain. A short latency response was evoked in DL by stimulating contralateral NO, but not following ipsilateral stimulation. Stimulation of DL evoked a response in the wulst of the same as well as of the opposite hemisphere. The latter had a longer latency.

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DECREASE IN THE NUMBER OF SYNAPTIC VESICLES AT CHOLINERGIC NERVE--ENDINGS FOLLOWING STIMULATION - V. Perri, E. Raviola, G. Raviola and O. Sacchi - Institutes of Gen. Physiology and Human Anatomy - University of Pavia - Italy

The distribution of synaptic vesicles, after prolonged stimulation of presynaptic fibres, was studied by electron microscopy, in more than one thousand nerve-endings of superior cervical ganglia excised from thiamin deficient rats and pair-fed controls. B_1 -avita minosis was tested as it is known to interfere with acetylcholine synthesis in the 'CNS. The vesicles were counted in the whole terminal and in restricted volumes at increasing distances from the synaptic contact. In the ganglia from control and B_1 -deficient rats, preganglionic stimulation produces a significant fall in the vesicle number both in the presynaptic ending as a whole and in the region where vesicles cluster against the presynaptic membrane. In unstimulated ganglia vesicle concentration does not decrease up to 4500 Å from the synaptic contact; after stimulation a progressive fall in the vesicle density is observed in this region, the fall being much more pronounced at some distance from the synaptic contact than in its immediate neighbourhood. During sustained stimulation vesicle supply is clearly inadequate to compensate for vesicle loss. B_1 deficiency, independently of stimulation, affects vesicle number only in the region closest to the synaptic contact.

THE EFFECT OF WATER DIURESIS AND ADH ON THE REGIONAL RENAL BLOOD FLOW.

Persson, A.E.G., J.Schnermann, H.R.Ulfendahl, P.Wunderlich and M.Wolgast.

Inst. of Physiology and Med. Biophys., Uppsala, Sweden and Inst. of
Physiology, Univ. of Munich, W-Germany.

The effect of water diuresis and ADH (arginine-vasopressin) on the cortical, outer medullary, and inner medullary circulation of 10 mongrel dogs was studied by intraarterial injections of labelled red cells. Indicator-dilution curves were registered with three separate semiconductor detectors mounted in a single needle device. The distance between the semiconductors was such that each detector was situated in one of the three kidney regions. The red cell flow was determined from 1) the mean transit time as calculated from the indicator-dilution curves, and 2) the regional red cell volume as calculated from the intrarenal equilibrium activity in relation to the blood equilibrium activity. It was found that water diuresis induced a moderate increase in red cell flow of all kidney regions, amounting to 24 %, 32 %, and 27 % in the cortical, outer medullary, and inner medullary region respectively. The injection of arginine-vasopressin reduced the red cell flow towards the control values parallel to the increase of urine osmolality. It is suggested that the effect of ADH on medullary solute concentration is partly due to reduced solute washout.

THE IMPORTANCE OF EXTRACELLULAR CO2/HCO3 FOR ACETYLCHOLINE-EVOKED SALI-VARY SECRETION. O.H.Petersen. Inst.Med.Physiol. C, University of Copenha-

gen, Denmark.

In the stimulated acini of the mammalian salivary glands an isotonic water transport occurs. In the gall-bladder and the proximal kidney convolution the isotonic water transport is dependent on the presence of $\rm CO_2/HCO_3^-$ in the extracellular fluid (Diamond, J.Gen.Physiol. 1964.48.1. and Rumrich & Ullrich, J.Physiol. 1968.197.69P.). In the perfused cat submandibular gland the salivary secretory rate during intraarterial infusion of acetylcholine was measured when the perfusion fluid contained $\rm HCO_3^-$ (25 mM) and was equilibrated with 5% $\rm CO_2$ in $\rm O_2$ and when the perfusion fluid did not contain $\rm CO_2/HCO_3^-$. A comparison of the secretory rates achieved with these two perfusion fluids in the same experiments revealed that there was no difference. Addition of acetazolamide ($\rm IO^-/M$) to the $\rm CO_2/HCO_3^-$ containing perfusion fluid did not inhibit secretion. The presence or absence of $\rm CO_2/HCO_3^-$ in the perfusion fluid was of no importance for the potassium transport between the gland and the perfusion fluid after acetylcholine stimulation and acetazolamide ($\rm IO^-/M$) did neither inhibit stimulation-induced potassium loss to the perfusion fluid nor active potassium uptake.

EXCITATION AND INHIBITION OF RETICULAR NEURONS AND RETICULAR SYSTEM. B.W. Peterson, L.P. Felpel, V.J. Wilson and M.E. Anderson. The Rockefeller University, New York City, U.S.A.

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Extracellular activity of medial ponto-bulbar reticular neurons has been recorded in chloralose-anesthetized, decerebellate cats. Trains of three shocks to precruciate cortex, labyrinths and skin typically evoked neural responses consisting of excitation followed by a 100-200 msec depression of firing. Preliminary intracellular recordings have shown responses consisting of an EPSP followed by long-lasting hyperpolarization caused in part by IPSPs. Earliest cortical excitation was monosynaptic, vestibular excitation was di- or polysynaptic. Reticulospinal neurons, identified by their antidromic responses to stimulation of the high cervical spinal cord, responded in the typical manner but were less likely to receive convergence of two or more inputs than were other reticular neurons. A spino-bulbo-spinal (SBS) reflex, evoked by stimulating lumbar dorsal roots and recorded in corresponding ventral roots, exhibited the same temporal sequence of facilitation and depression following a conditioning stimulus as did reticular neurons. Fluctuations in excitability of the SBS reflex from trial to trial were also correlated with fluctuations in excitabilily of reticular neurons. These results indicate that input to the medial reticular formation can strongly influence activity of at least one pathway controlling motoneuron excitability. Supported in part by USPHS Grants NS 02619 and NS 05463.

A SYSTEMS APPROACH TO PHYSIOLOGY. L.H.Peterson, R.Cox, A.Jones, G.Karreman, G.Fischer, R.Bagshaw, J.Pace. Bockus Research Inst., Univ. of Pennsylvania, Philadelphia, Pennsylvania, USA.

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The complexity of physiological systems is one of the major problems in studying and-understanding them. Thus, one of the major challenges to physiology is to learn how to understand the properties and behavior of complex systems, i.e., those involving many variables and parameters and their complex interactions. An approach increasingly used is that of systems analysis and computer modeling and simulation. Indeed, there is no other known way to conceive of, evaluate, and understand complex systems except intuitively. The circulatory system is one of great complexity, involving nervous, endocrine, renal, et cetera functions as well as cardiovascular functions. The Bockus Institute, during the past seven years, developed a computer model of the circulatory system involving the interaction of nervous, endocrine, renal and cardiovascular functions and containing more than 100 functions. The model not only represents and tests current physiological concepts about the circulation but also provides insight into the systems aspects of multi variable, multi feed-back loop control and regulation. This approach has provided new insight into physiological controls and has also provided an applied methodology for determining a control system for artificial hearts. Additionally, it has provided insight into the systems aspects of the regulation of the circulation in hypertension. Supported in part by USPHS HE 07762 and Office of Naval Research Grant N ONR 551(54).

DATA INDICATIVE OF THE EXISTENCE OF SEROTONIN RECEPTOR CONSTELLATION.

V.Petkov. Postgraduate Med.Inst., Dept.of Pharmacology, Sofia, Bulgaria.

A large number of substances are known which belong to quite different chemical and pharmacological groups and block the serotonin receptors. On various isolated organs, it was established that agonists and antagonists of the same type, interacting with various receptors (noradrenaline and phenoxybenzamine, isopropyl-noradrenaline and propranolol, etc.) in proportion to the concentrations used, shift the serotonin concentration effect curves along the concentration axis to higher concentrations. The combined application of either two agonists, or an agonist and an antagonist, both acting as serotonin antagonists, results in an attenuation of the serotonin effect. On the other hand, both serotonin and benzyloxygramine attenuate the effects of substances which belong to different pharmacological groups. On the whole, therefore, one has every reason to presume that serotonin interacts with a constellation of receptors.

1337 CARDIOVASCULAR AND RESPIRATORY RESPONSES TO ECHIS CARDINATUS VENOM AND ITS FRACTIONS. D.Petkovic. Dept.of Physiology, Faculty of Medicine, University of Khartoum, Sudan.

The effects of Echis Carinatus venom and its chromatographic fractions were investigated on the blood pressure, E.C.G. and respiration of rabbits. Five fractions of the venom were obtained by column chromatography using Sephadex G-100. The venom produced a triphasic change in the blood pressure. This consisted of an initial fall, followed by a slight rise and then abrupt fall which continued until the animal died. These changes in blood pressure could not be antagonized by atropine or mepyramine. The E.C.G. showed slowing of the heart, spiky T waves and various degrees of heart block. Respiration became deeper and irregular but it continued for sometime after the circulation has stopped. Fraction 4 of the venom produced similar changes as the whole venom. The other fractions had no effect. These results show that death in Echis Carinatus envenomation is mainly due to circulatory failure and that fraction 4 of the venom is responsible for these changes.

1338 INTRAVASCULAR PRESSURE AND RESPONSIVENESS OF THE SMOOTH VASCULAR MUSCLE IN VIVO. L. Petrov, St. Gagov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

In acute experiments with cats studies were made on the constriction response of the vascular bed of the limb upon intraarterial injection of a standard amount of noradrenaline. By a pulse pump with a constant flow the vascular bed was perfused at different levels of the pressure. Evidence was presented to show that under the conditions of normal and basal vascular tone the constriction response appeared at a pressure of 50 to 60 mm Hg and upon increasing the pressure it began to subside continuously. Under the conditions of decreased basal tone, after intraarterial injection of papaverine, the constriction response appeared at a higher pressure, as first it increased with increasing the pressure and later it began to decrease.

GASTRIC ACID SECRETION IN THE FERRET DURING ESTRUS AND ANESTRUS. C. J. Pfeiffer and C. M. Peters. Inst. of Gastroenterology, Presbyterian-U. of Pa. Med. Ctr., Philadelphia, Pa., U.S.A. Basal and stimulated gastric hydrochloric acid secretion was studied in

22 chronic fistula ferrets during estrus and anestrus. Maximal doses of histamine (67.3 μ g base/kg, I.P. and S.C.) pentagastrin (10 μ g/kg, I.P.) or insulin (1.5 U/kg, I.P.) were administered to stimulate secretion after basal secretion was assessed. Basal secretion was unaltered by estrus. Acid output, concentration (pH 7.4), and volume output after intraperitoneal histamine were unaltered by estrus, but peak concentration and volume were slightly increased (p<0.02) after subcutaneous histamine during estrus, suggesting that a hepatic factor, related to route of administration, may have altered the histamine effect. Pentagastrin and insulin-induced may have altered the histamine effect. Pentagastrin and insulin-induced stimulation were slightly increased (p < 0.05) during estrus in terms of acid concentration, but acid output and volume were unchanged. Histamine and pentagastrin responses were rapid, response kinetics generally following the pattern $\log Y = a + b (\log X) + c (\log X)^2$. Peak responses in gastric secretion after insulin were delayed and sustained, following the pattern $Y = a + bX + cX^2$. The present study suggests that natural hormonal changes may slightly alter the gastric secretory responses to test agents in the ferret.

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DEPENDENCE OF HYPOSMOTIC FLUID TRANSPORT ON ION MOVEMENT WITHIN RECTAL EPITHELIUM OF LOCUSTS. J.E. Phillips, University of British Columbia, Vancouver, Canada.

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The desert locust, which lacks the anatomical equivalent of the mammalian kidney counter-current system, produces strongly hyperosmotic excreta. This is achieved by net water absorption across the rectal epithelium against increasing osmotic gradients (i.e. absorbate is hyposmotic). On ultrastructural grounds, it has been postulated that this transport of water is driven by (i.e. coupled to) solute re-cycling across the lateral membranes of the epithelium, although previous studies failed to demonstrate dependent of water transfer on ion transport. This hypothesis was tested by studying the effects of altering the ionic composition of the bathing medium on the steady-state rate of water transport (also absorbate composition) by the in vitro rectum, previously depleted of tissue ions by incubation in isosmotic sucrose. While ions on the lumen side are required for prolonged transport of water, there is no absolute requirement for any single monovalent ion. Amino acid transport was demonstrated for the first time in insects but this cannot account for water transport. Total concentration of free amino acids, urea, and inorganic ions in the rectal tissue is similar transport of water, there is no subject to the first time in insects but this cannot account for water transport. Total concentration of free amino acids, urea, and inorganic ions in the rectal tissue is similar to that of the blood and to low to create a favorable osmotic gradient for simple osmotic flow across the apical membrane, as required by the recycling hypothesis. However, these experiments provide the first direct evidence that hyposmotic fluid transfer in the insect rectum is coupled to

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STUDIES ON THE SYNTHESIS OF GLYCOGEN IN BRAIN SLICES. Mary E. Phillips and R.V.Coxon. Univ.Lab.of Physiol.Oxford, England.

The experiments to be reported were designed to throw some light on possible factors affecting the synthesis of cerebral glycogen and were performed using slices of guinea-pig brain incubated in vitro. Among the factors studied were two hormones (insulin and hydrocortisone), variations in glucose availability and the presence of potential precursors other than glucose. No effect of such precursors on the net synthesis of glycogen could be demonstrated nor could any positive effects from the hormones which were tested. On the other hand some incorporation into glycogen of isotopic carbon presented to the tissue in the form of pyruvate, glutamate and bicarbonate was found. The interpretation of these findings will be discussed, together with some differences noted in vivo between the behaviour of cerebral glycogen in guinea-pigs and that in other animal species.

1342 UNIT ACTIVITY RESPONSES TO POSITIVELY AND NEGATIVELY CONDITIONED AUDITORY STIMULI IN RATS. M. Ian Phillips, Dept. Physiology, Univ. Iowa, Iowa City, Ia. 52240, U.S.A.

This study is a continuation of the finding that mesencephalic reticular formation (RF)units make discriminatory responses to positively conditioned stimuli(CS)(Phillips & Olds, Science, 165, 1269,1969). Using Olds'technique, 26 rats had 4-6 microelectrodes implanted chronically for simultaneous recording of different brain sites. Movement was also recorded at 50 msec intervals during the 1 sec pre- and 1 sec post-stimulus poriods. Pseudo-conditioning, conditioning and extinction trials were given (300 of each of 2 tones presented at random). RF units(60%) showed discrimination with lower responses to the shock-CS and higher ones to the food-CS and vice-versa in 2 cases. The responses preceded similar responses made by rats' movements. Units in the inf. colliculus, lat. hypothalamus and dors. thalamus showed sensitisation to the tones and no discrimination. Med. geniculate units(80%) made discriminated responses. The results show that certain units may distinguish between positive and negative CSs irrespective of the frequency of the tones used and that discrimination of auditory input is possibly present at the med. geniculate level. (Work was done in the lab. of J. Olds(Caltech) to whom I am grateful for his interest and support, USPHS grants)

MODE OF ACTION OF TETRAETHYLAMMONIUM (T.E.A.+) IONS ON INSECT NERVE MEMBRANE. Yves Pichon. Dept. of Zoology, University of Cambridge (U.K.).

Insect nerve membrane resembles squid nerve membrane except on its sensitivity to externally applied T.E.A.+. The present study has been carried out in order to obtain a better idea on the mode of action of this ion on insect nerve membrane. Special attention has been paid to the possibility for T.E.A.+ to cross the membrane using the normal sodium (Na+)'channels' before acting on the potassium (K+) 'channels' from inside as it does in squid axon. Intracellular recording from giant axons in the abdominal connectives of Periplaneta americana using microelectrodes as well as external recording and control of the membrane potential of a small area of an axon isolated from this same preparation have been used throughout this work. (1) When applied to the giant axon of the cockroach, T.E.A.+ (25 mM/1) reduced K+ conductance, thus inducting a depolarization of about 5 mV and a lengthening of the falling phase of the spike, This effect was fully reversible. (2) Repetitive stimulation of the preparation does not affect the time course of the T.E.A.+. induced depolarization neither the kinetics of the change in the falling phase of the action potential. (3) Raising external calcium (Ca++) from 1.8 to 10 mM/1 had a noticeable effect on the action potential but did not inhibit the effect of T.E.A.+. (4) Replacement of all the Na+ by T.E.A.+ gave rise after stimulation to T.E.A.+ action potentials or T.E.A.+ transient inward current, a current which was abolished by tetrodotoxin whereas the K+ current was still reduced. These results will be discussed in terms of external or internal location of T.E.A.+ 'sites'.

TEMPERATURE EFFECTS ON SPIKE PARAMETERS AND RESTING POTENTIAL IN MOTONEURONS F.-K. Pierau, M.R. Klee, D.S. Faber, Kerckhoff-Institut d. MPG, Bad Nauheim, and MPI Hirnforschung, Neurobiol. Abt., Frankfurt (M), Germany.

To test the sensitivity to temperature of the active Na⁺/K⁺ transport

To test the sensitivity to temperature of the active Na*/K* transport system of cat lumbosacral motoneurons, differential recording of RMP, membrane resistance (Rm), antidromic action potential and its electrical differentiation (dV/dt) were made during local temperature changes for 10-20 min. During cooling from 38-29°C, RMP decrease was inversely related to the initial value of RMP. Time constants of the afterpotential were increased (10-40%), while its amplitude was relatively unchanged. Simultaneously Rm increased by 30%. Spike amplitude decreased and duration increased; however, the spike overshoot frequently increased despite the depolarisation and reductions in the 4 peaks, E₁-E₄, of the dV/dt records. E was often unchanged the reduction of E, was significantly less than that of E,. The overshoot increase can be attributed to the 2 times greater Q₁₀ of K* activation and inactivation than that of Na* in toad nerve fibres. During rewarming, all parameters returned to normal, albeit with a hysteresis, and often with an initial transient increase in RMP. In the temperature range and with the durations used, these results can be explained by the differentials in temperature sensitivity of P_{K+} and P_{Na+} and of the conductance changes during a spike, but they seem not to be caused by changes in the Na*/K* pump.

ANALYSIS OF THE RESPONSE OF ISOLATED FROG TONGUE PAPILLAE TO DIFFERENT CHEMICAL STIMULI. P. Pietra, V. Taglietti and A. Miraldi. Inst. of General Physiology, University of Pavia, Pavia, Italy.

1345

In an attempt to investigate the functional interaction between individual components of the frog tongue taste receptors system, a technique for dissecting the lingual mucose has been developed. This preparation enables a single taste papilla to be chemically stimulated in isolation from those surrounding it and the discharge of impulses evoked by stimuli to be picked up from the bundle of fibres innervating that papilla. The action potentials were recorded on magnetic tape and fed into a CAT 400 C apparatus, which allowed the analysis of intervals between the impulses occurring during discharges. Data were then processed on a DEC PDP-8/L computer. Preliminary findings using this procedure indicate that some stimulating substances, such as CaCl₂ solutions, give rise to a random sequence of impulses, whereas others, such as BaCl₂, H₂SO₄ and Tiourea solutions, evoke specific discharge pattern which can be related to the kind of chemical stimulus used.

RESTORATION OF SYNAPTIC TRANSMISSION IN THE DENERVATED AVIAN CILIARY GANGLION. G. Pilar and L. Landmesser. Dept. of Physiology, University of Utah, SLC, Utah 84112, U.S.A.

1346

Presynaptic fibers were cut 2 mm proximal to the adult pigeon ciliary ganglion. The modification of transmission in the ciliary and choroid cell populations was studied after periods of 6 hours to 100 days. Axon counts of the presynaptic and postsynaptic nerves were made in controls and in preparations obtained 3 to 6 months after nerve section. Transmission was restored after 13-15 days. Regenerated presynaptic cliiary fibers had faster conduction velocity and lower threshold than presynaptic choroid fibers, restoring the control situation. Electrical transmission reappeared in four weeks solely in the ciliary population. Nerve fibers innervating the extraocular muscles also regenerated achieving conduction velocities similar to control values. While regeneration was thus highly selective, ganglionic transmission measured electrophysiologically was only 10-20% restored. There were 5-10% fewer postsynaptic axons in the regenerated ciliary and choroid nerves, and approximately the control number of total oculomotor nerve fibers proximal to the nerve section. However, there was a 10% reduction in total oculomotor fibers distal to the nerve section, but there was no reduction of regenerated extraocular motor fibers. The decreased number of axons in presynaptic nerves can only partially explain the incomplete restoration of transmission. Other explanations may be subthreshold innervation of most of the ganglion cells, or persisting non-functional inappropriate synaptic connections.

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METABOLIC CONVERSION OF GLUTAMINE BY THE KIDNEY OF THF DOG. Lou Ann Pilkington. Department of Physiology, Cornell University Medical College, New York City.

1347

The utilization of glutamine for the production of ammonia, for the formation of glucose and for oxidation to CO₂ was studied in slices of the cortex of kidneys of dogs made acidotic or alkalotic in vivo and from slices of normal dog kidneys made acidotic or alkalotic in vitro by changes in composition of the incubation medium. In slices made acidotic in vitro the amount of glutamine converted to CO₂ was five to six times greater than the amount of glutamine converted to glucose. Relative to the amount of ammonia produced, these two pathways of utilization constitute the major metabolic fates of glutamine. In dogs made acidotic in vivo, production of glucose from two substrates in combination, glutamine plus α -ketoglutarate, glutamine plus pyruvate or glutamine plus lactate, was two to four fold greater than that observed from glutamine alone. Thus, the gluconeogenic pathway is not rate-limiting for utilization of glutamine. The rate of production of ammonia from glutamine was inhibited 85% by addition of α -ketoglutarate. We conclude that the major metabolic fate of glutamine is conversion to CO₂. Supported by NIH grants.

ANOMALIES OF FAT MOBILIZATION IN THE OBESE. A KINETIC STUDY OF FFA. E. J. Pinter Queen Mary Veterans Hospital, Montreal, Canada.

Fat mobilization was studied in 119 obese and lean subjects at rest and under a) nutritional (starvation) and b) non-mutritional stimulation (epinephrine, pyrogen,emotional stress, post iv nicotinic acid and phenoxybenzamine FFA rebound). FFA production (Ra), utilization (Rd) and pool (N) were measured in 33 subjects. These data were correlated with: weight, body surface area, adipose tissue and lean body mass. Conclusions:

1) In all studies FFA production rates were the primary determinants of FFA levels and pool sizes. The relative magnitude of total FFA utilization was always comparable between lean and obese. 2) At rest: fat mobilization is proportional to body weight; there is hyperadipokinesis in obese in relation to their lean body mass and viz the lean. 3) In starvation: Ra and N (as/body surface or lean body mass) are virtually equal in lean and obese. Increments of Ra and N viz resting values are significantly smaller in obese, however. 4) In non-nutritional stimulation the obese show significant overproduction of FFA in relation to their lean body mass viz the lean. 5) Fat mobilizing capacity of obese is adequate; the adipokinetic anomaly is explained by distorted adipose tissue/lean body mass relationship and cannot be causally related to the development of obesity.

1349 TIME COURSE OF LIGHT-INDUCED CHANGE IN RESISTANCE OF RETINAL RECEPTOR CELLS. Pinto,
Lawrence H. & Pak, William L. Dept. of Biol. Sciences, Purdue University, Lafayette, Ind.

The response of vertebrate receptor cells to light stimulation consists of hyperpolarization accompanied with increased membrane resistance. One proposed explanation for receptor potentials is: during illumination net current is modulated by decreasing the conductance for only the inward component of current flow. If this is so, then it follows that the time course of the change of resistance of the membrane should be the same as that of the response. This work is intended to measure precisely both time courses. Resistance change and voltage measurements were made upon single cells of the Gecko gecko and Tiger salamander using hyperfine pipettes filled with Procion Yellow or K Cl and sellected for stable, low resistance (100 - 250 M ohm). Resistance measurements were made with the aid of a constant current clamp and a lock-in amplifier and averaged; response waveforms were similarly averaged. Preliminary results from four cells of the Tiger salamander (pipette probably in inner segment) show that the latency of the resistance change is at least 0.1 sec longer than that of the response and the time constant of the resistance change at least 0.4 sec greater than that of the response. Such differences have not been noted in four cells of Gecko gecko (pipette probably in outer segment). These results suggest that the above hypothesis requires modification and are now being confirmed with dyes which permit intracellular localization of the pipette tip.

1350 RENAL EXCRETION IN CONDITIONS OF OSMOTIC DIURESIS. B.G.Piryova Inst. of Physiology, University of Medicine Sofia, Bulgaria.

The renal function in dogs is investigated after infusion of a hyperosmotic solution of manitol at various rates. A linear dependency is found between the rate of increase of the diuresis and osmotic excretion and the rate of infusion. The renal function is estimated on the basis of the maximum water excretory capacity (50% GFR) and the maximum osmotic excretory capacity ($T^0_{H_2O}$ + 50% GFR) in the given conditions. The kidney utilizes its water capacity to a greater extend than it does utilize its osmotic capacity. The rate of increased utilisation of the excretory capacity is greater for water excretion than for osmotic. The percenage of utilized water and osmotic capacities is a linear function of the quantity of non-excreted osmo-active substances up to 10 mOsm/kg.

MEASUREMENT OF MOLECULAR WEIGHT ON 10⁻⁷g SAMPLES OF PROTEINS. J.C. Pita, F.J. Muller and L.A. Cuervo, Dept. of Medicine, Univ. of Miami School of Med., Miami, Fla.

1351

Practical curves and nomographic charts have been constructed for the evaluation of S and D coefficients at an ultramicro level by the transport method. 200 nl of solution with protein concentrations as low as 0.5mg/ml were centrifuged at high speed in small capillary cells, (0.3 mm in diameter and about 3.0 mm total length). The micro cells were sectioned after the centrifugation-diffusion process through a previously marked plane on the glass surface. Analysis of solute concentration in the supernatant, (upper section), and bottom, (lower section), allowed determination of S and D values within 5% experimental error. The curves were obtained by numerical approximation of the diffusion-sedimentation process with the aid of a computer. Limitations of this method lie only in the precision of the analytical assay.

The method was verified experimentally, by using proteins of known diffusion and sedimentation constants such as lysozyme, ovalbumin, human serum albumin and phosphorylase B. Typical results obtained are: $S=4.55_3 \times 10^{-13}$ sec. and $D=6.24_3 \times 10^{-13}$ sec for human albumin. For lysozyme $S=1.85 \times 10^{-13}$ sec. and $D=1.20 \times 10^{-6}$ m sec . These values are in satisfactory agreement with published data...........

CHRONOLOGICAL RELATIONSHIP BETWEEN PLASMA LUTEINIZING HORMONE AND PROGESTERONE LEVELS DURING THE NORMAL MENSTRUAL CYCLE. M. Pizarro, K. Thomas and J. Ferin. Physiology of Human Reproduction Res. Unit, Univ. Hosp., B-3000 Louvain, Belgium.

1352

In ten normal women, 20-36 year old, blood was collected daily during the whole menstrual cycle or at midcycle. In two volunteers blood was obtained every 4-6 hours during the suspected periovulatory period in order to document more precisely rapid hormonal variations occurring at that moment. Determinations were carried out simultaneously on all plasma samples of a given volunteer, relying on a radioimmunological technique for luteinizing hormone (IH) and on a competitive protein binding method for progesterone. (1) Plasma IH profile was characterized by a sharp mid-cycle peak, lasting about 48 hours and occurring just before or during the thermal shift. During the follicular phase, 'basal' IH concentrations were not significantly different from those found in the luteal phase. (2) Progesterone levels remained low during the follicular phase, increased at the very onset of the IH discharge, reached a maximum by the middle of the luteal phase and dropped toward follicular levels at the end of the cycle. (3) During the periovulatory period, progesterone levels were found to rise as soon as the increase in IH titer could be detected, attaining a plateau through the IH surge; after a slight, short-lived drop, they increased to the luteal peak. It may be suggested that this early phase of progesterone secretion acts as a 'trigger' involved in the IH surge.

1353

PROPERTIES OF SOMATO-SYMPATHETIC INHIBITION. C.Polosa and I.Wyszogrodski. Dept. of Physiology, McGill University, Montreal, Canada.

Background spike activity of single, antidromically identified, sympathetic preganglionic units (SPU), was recorded with extracellular glass micropipettes in the upper thoracic cord segments of cats. In CNS-intact, Nembutal anesthetized and mid-pontine decerebrate un-anesthetized preparations, single supramaximal shocks to the central cut end of the sciatic nerve evoked a suppression of background firing, not preceded by excitation, in 8 out of 20 SPU (40%). Average latency and duration of this response were 150 msec (range 60 to 300) and 700 msec(range 280 to 1200) respectively. In acute, C-1 spinal preparations, Nembutal anesthetized or decerebrate un-anesthetized, single supramaximal shocks to the sciatic nerve also evoked a suppression of background firing, not preceded by excitation, in 5 out of 12 SPU (42%). Average latency and duration of this response were 110 msec(range 50 to 180) and 650 msec(range 250 to 1100) respectively. Drugs which were effective in modifying the inhibitory response in the CNS-intact and decerebrate preparations were also effective in modifying the inhibitory response of the spinal preparation. The similar properties of the inhibition in the spinal preparations and in the preparations with intact CNS or with mid-pontine decerebration suggest that the circuitry of this inhibitory reflex is mainly spinal. (Supported by the Medical Research Council of Canada).

1354 TISSUE RESPIRATORY CHANGES INDUCED BY INCUBATION IN Na -FREE MEDIA. F. PONZ and R. JORDA-NA, Dept. of Physiology, University of Navarra, Pamplona, Spain.

Strips of rat jejunum were incubated in several isoosmotic Na -free media, containing mannitol, sucrose, Li⁺, choline or Tris as substituents for Na⁺. In all cases, inhibi tion of oxygen consumption was observed, increasing with time (3 hrs.), and it was different for each substituent, being highest for mannitol or sucrose (60-70 %) and lowest with choline. Respiration was inhibited in Na $^+$ containing medium when strips had been preincubated (60 min.) in Na+-free media, but only if its substituent was either man nitol or Li+. Similar results were obtained with rat liver slices. In this case the stronger inhibitions were found with mannitol, sucrose or glucose. After preincubation in the absence of Na⁺, the oxygen uptake became almost the same as those for the controls except when the substituent had been mannitol or K+. Na+ substitution by non-electrolyte substances diminishes the succinate dehydrogenase activity of the tissues. The observed respiratory changes are not exclusively due to the absence of Na^+ but also to other factors depending on the nature of the Na^+ substituent.

WORK PSYCHOPHYSIOLOGY RESEARCH IN THE MECHANIZED AND AUTOMIZED INDUSTRY. 1355

Aurelian Popescu. Institute for Normal and Pathological Physiology, Academy of Medical Sciences, Bucharest, ROMANIA.

A complex methodology of psychophysiological investigation was used within the researches undertaken in some spheres of the mechanized and automized industry, able to lead to the dynamic catching of the human body's reactions, engaged in several forms of the productive work as follows:

1) The analysis of the work processes; 2) The psychologic study; 3) The study of the superior nervous activity dynamic. The research underlines the essential differences that appear in the two types of activity. The mechanized work (the running bett etc.) characterized by the imposed rythm where the cooperation of the visual and motor analysator prevails sollicits especially the function of coordination and presents modifications in the sector of attention, memory and affectivity depending on the characteristics of the nervous system type and as a consequence of the appearence of tiredness. Unlike the mechanized work, the activity in the automized sectors is characterized by the simultaneous pursuit of move processes that change in time and by its abstract characters at which is added the growing of speed on a ennity of time, the state of start and mized industry, able to lead to the dynamic catching of the human body's added the growing of speed on a ennity of time, the state of start and the posture effort.

1356 EFFECT OF AMINO ACID IMBALANCE ON SOME LIVER ENZYMES. Aurora Popescu, M.D.Mezincescu, Marilena Fărcașiu, Lizica Croitorescu. De gical Chemistry, Faculty of Medicine. Bucharest, ROMANIA. Departm. of Biolo-

As a contribution to the understanding at metabolic level of amino acid imbalance, the activities of 8 rat liver enzymes were estimated in 3 types of imbalance. Type I imbalance (4 experiments) was induced by addition of 12% gelatin to a basal diet comprising 8% casein. Imbalance of type II (experiments) was provoked by addition of 0.6% methionine + 0.9% phenylalanine to a basal diet containing 6% fibrin. Type III imbalance (5 experiments) was produced by addition of 0.6% threonine to the basal diet with 8% casein. S-amino acid oxydase activity was influenced only by type I imbalance, being lower in imbalanced animals. Xantine oxydase and succinic dehydrogenase activities increased in type II imbalance and were not affected by the other types of imbalance. Aldolase, lactic dehydrogenase and alkaline phosphatase activities were influenced by imbalances of types I and III, being much lower in the imbalanced rats. Acid phosphatase activity was lower in all three kinds of imbalance. phosphatase activity was lower in all three kinds of imbalance.

A STUDY ON THE ADAPTATION OF THE BIOLOGICAL RHYTHM TO DIFFERENT TYPES OF EFFORT IN WOMEN. <u>Dr.G.Popescu and Dr.O.Luchian</u>. Gynaecological-Obstetrical Clinic of "Brîncovenesc" Hospital, București, Romania.

1357

In this study the authors consider the specific factors influencing the capacity of women to effort with different work-loads. On a representative sample of 112 women and a normal sample of 70 women the stages of the menstrual function correlated with the gynaecological morbidity and neurovegetative balance were studied. The correlation between the capacity to effort and the stages of the menstrual function (pre-inter-post) evidenced that the latter have a different impact on the capacity to effort as a function of the gynaecological health condition and the hormonal characteristics of the monthly flow. The post-menstrual stage is the best one for any kind of activity. The neurovegetative functions which were studied on effort and at rest on the same sample revealed the appearance of some sense and motor alterations closely connected with the type of menses and the presence or absence of gynaecological diseases.

HEXOKINASE AND PYRUVATEKINASE ACTIVITY IN THE RAT LIVER AND KIDNEY UNDER THE INFLUENCE OF ANTIBIOTICS. G.G.Popovici, C.Mungiu, M.Trandafirescu, E.Botez, D.Cernätescu, D.Caraman. Dept. of Pharmacology and Dept. of Biochemistry, Inst. of Medicine, Iași, Romania.

1358

The possible intervention of some antibiotics in certain compartments of the intermediary metabolism of carbohydrates in various animal tissues was demonstrated in previous investigations. This paper reports the influence of the antibiotics on the activity of hexokinase and pyruvatekinase, enzymes with a limiting and regulating role in glycolysis and determinants of the cell energy potential. The influence of the antibiotics upon the activity of these two enzymes was followed up in the rat liver and kidney, in vitro and in vivo. Determinations were done spectrophotometrically at 340 nm, with the help of G6PDH and NADP for hexokinase and with LDH and NADH2 for pyruvatekinase. The results obtained showed that streptomycin, neomycin and chloramphenical modify the activity of the two enzymes in both organs, whereas penicillin and erythromycin exercise no significant influence. Differences sometimes exist between the in vitro and in vivo effect produced by some antibiotics. The changes observed show that especially streptomycin and neomycin may limit the utilization of glucose in intermediary cellular metabolism and ATP synthesis.

1359

REPETITIVE FIRING IN RECEPTOR NEURONS. R. E. Poppele and R. L. Purple. Laboratory of Neurophysiology, Univ. of Minnesota, Minnesota, Minnesota, U.S.A.

Repetitive firing of receptors has been studied using the technique of systems analysis in the mammalian muscle spindle and in the slowly adapting stretch receptors of the crayfish. In these cells, generator currents cause repetitive firing which can be modeled by a process which charges to threshold with a characteristic time constant. In the neurons studied, this time constant is not the membrane RC, and it is inversely related to the magnitude of generator current. The results suggest that in repetitively firing neurons, there is a nonlinear process responsive to generator current that determines the time constant of repolarization following each spike. (Supported by Grants from USPHS - NS 07421 and EY 00293.)

ISOLATED ANTERIOR PITUITARY CELLS: A MORPHOLOGICAL AND FUNCTIONAL STUDY. R. PORTANOVA and G. Sayers, Case Western Reserve University, Cleveland, Ohio, U.S.A.

Trypsin dispersed anterior pituitary cells have been characterized by morphological and functional technics. Electron micrographs show the plasma membranes are intact and welldefined, mitochondria and other intracellular organelles are normal in structure and secretory granules are present. Suspensions of the cells contain all the recognized pituitary cell types. Coated invaginations of the plasma membrane are observed and secretory granules are occasionally seen within such invaginations. These findings are consonant with the view that release of adenohypophysial hormones is mediated via bulk transport processes. The functional integrity of the cells is indicated by several criteria. They contain ACTH in a concentration per cell mass approximately equal to that of pituitary tissue fragments and under control conditions retain the hormone against a large concentration gradient. The release of ACTH is promoted by extracts of rat hypothalamic median eminence (HME), vasopressin, and excess potassium or zero calcium in the incubation medium. In the case of HME and vasopressin, the response is inhibited when calcium ion or glucose is omitted from, or when physiological amounts of corticosterone are added to the incubation medium. The cells catalyze the incorporation of radioactive amino acids into protein. Omission of glucose from, or addition of puromycin to the incubation medium inhibits this process. These findings indicate that trypsin-dispersed anterior pituitary cells may be useful for studying the metabolism of adenohypophysial hormones. (PHS Grant No. AM 13820)

1361 ATP-INDEPENDENT CALCIUM TRANSPORT IN HUMAN ERYTHROCYTE GHOSTS. H. Porzig. Dept. of Pharmacol., Univ. of Berne, Switzerland.

Only in ATP loaded red cell ghosts an active uphill Ca transport can be measured. However, even in the absence of ATP, using Ca⁴⁵ as a tracer, the following findings indicate the existence of a specific Ca transport system facilitating Ca-Ca or Ca-Sr exchange: (1) The unidirectional efflux increases and shows saturation kinetics when [Ca]o is increased stepwise from 0 to 4mM/1, while [Ca]o remains constant. (2) The same relationship exists between efflux and [Ca]i when [Ca]o remains constant. (3) The unidirectional influx increases and shows saturation kinetics when both [Ca]o are increased simultaneously. (4) Addition of Sr to the outside induces a countertransport of Ca against a gradient. The system does not seem to operate symmetrically on both sides of the membrane since the rate constants for efflux and influx depend more on [Ca]o than on [Ca]o. Direct determinations of [Ca]o in the presence of different inwardly directed gradients for Ca indicate that the system has a steady state far from chemical equilibrium. Moreover if [Ca]o is higher than [Ca]o, the net uptake of Ca is smaller than the net loss in presence of the same but outwardly directed gradient. Thus the erythrocyte membrane seems to have some rectifying properties for Ca transport.

1362 EXCITATORY AND INHIBITORY ACTIONS OF NOREPINEPHRINE ON POTASSIUM TRANSPORT IN CARDIAC PURKINJE FIBERS. P. POSNER AND M. VASSALLE. Dept. of Physiology, State University of New York, Downstate Medical Center. Brooklyn, N. Y., U. S. A.

The aim of the present study was to investigate the actions of different doses of norepinephrine on potassium transport in cardiac Purkinje fibers and some of the characteristics of these actions. The preparations were perfused in a tissue bath in close proximity to a beta probe and loaded to equilibrium with ⁴²K. Tissue radioactivity and transmembrane potentials were measured simultaneously. It was found that 2.5 x 10⁻⁵M norepinephrine stimulated while 2.5 x 10⁻⁴M inhibited K uptake in the same preparation. Both stimulatory and inhibitory effects of norepinephrine were abolished by substituting Na⁺ with choline. The inhibitory effect was present in both driven and quiescent fibers and was blocked by either the removal of CaCl2 from the perfusate or by pretreatment with the alpha blocker Regitine in both driven and quiescent fibers. It is concluded that excitatory and inhibitory effects of norepinephrine on K transport depend upon the concentration of the amine. Both effects require the presence of Na⁺ and the inhibitory effect also that of Ca⁺⁺. The inhibition is an alpha function.

Supported by grants from the Research Foundation of the State University of New York and the New York Heart Association.

EXPERIMENTAL AND THEORETICAL STUDIES OF THE LUNG AS AN ELASTIC STRUCTURE. W.R. Powell, J. Billingham and M. Anliker. Ames Research Center, NASA, Moffett Field, Calif. 94035, U.S.A., and Stanford University, Stanford, Calif. 94305, U.S.A.

An improved model of the mechanical behavior of the mammalian lung is developed which describes both the pressure-volume and weight-volume behaviors. Weight changes due to pulmonary blood volume changes cause alterations in gravity stresses which may affect the mechanical behavior of the lung and possibly explain the localization of diseases such as emphysema.

The lung is divided into four components, the lung tissue, the pulmonary blood volume, the alveolar gas volume and the bronchial tree gas volume. Each of these components contributes to the mechanical behavior of the lung. The lung tissue is modeled as an incompressible material which constitutes approximately one half of the lung weight under normal conditions. Experimental studies on excised canine lungs show that the pulmonary blood volume varies directly with transpulmonary pressure and with the gas volume in the lung for quasi-static inflations. The pulmonary blood volume changes decrease with respiratory frequency and are no longer measurable above 15 cycles/minute. The behavior of the alveolar gas volume is obtained by modeling each alveolus as a spherical bubble on a cylinder. A new description of tissue stresses is given on the basis of recent experimental results using a nonlinear stress-strain relationship. Experimental pressure-volume studies of the bronchial tree indicate that the tree behaves like the alveoli.

The four components combined produce a mechanical model which agrees well with the observed pressure-volume behavior of excised canine lungs. The model predicts that the lung weight increases by 1/4 during inflation and that gravity stresses in alveolar walls are of the same order of magnitude as are the stresses due to the transpulmonary pressure.

MODIFICATION OF INSTRUMENTAL CONDITIONED RESPONSES BY ATROPINE, ACETHYLCHOLINE, EPINEPHRINE OR NOREPINEPHRINE APPLIED IN THE CAUDATE NUCLEUS (CN) OF CATS. R. Prado, J. Grinberg (1) and H. Brust-Carmona. Dept. of Physiology, Sch. of Med., Nat. Univ. of Mexico, México 20, D. F. (1) Psychol. Sch. Univ. Anahuac, México State, México. Previous work showed that partial lesion of the CN depressed the conditioned inhibition

Previous work showed that partial lesion of the CN depressed the conditioned inhibition of the motor conditioned response (ICR), with almost no effect in the motor conditioned response (CR). It was also found that the spreading depression evoked by KCl 3 M. in the CN abolished in a reversible way the CR. Since that indicated that the CN has a very important role in the integration or in the performance of these types of CR and ICR, we decided to investigate the effects of possible transmitter substances on the same learned responses. The experiments were performed in adult cats. They were conditioned to stay inside a cage until the CS appeared (4 flashes, l/sec.), they then walked to the other end of the table, got a reward and went back to the cage (CR). When the CS was associated to 4 clicks there was no reward, thus the Ss learned to stay in the cage (ICR). When the Ss had learned both responses cannulae were stereotaxically implanted in the CN. The daily trials were divided in three series. Ramdomly between the first and second series a sham or a real microinjection of saline solution or a test substance was made. The results indicate that atropine (80 microgr. in 0.005 ml.) blocked the CR completely in the first 5-6 applications but had less effect in consecutive applications. Ach produced variable results but showed a tendency to improve the CR. Epinephrine and norepinephrine in doses of 4-8 microgr. improved the ICR without altering the CR; however, the CR was blocked with 16 microgr.

GLUCAGON AND OUABAIN ON THE TRANSMEMBRANE POTENTIAL, CONTRACTION AND ATPase ACTIVITY OF HUMAN HEART. K. Prasad, Dept. of Pharmacology, Univ. of Alberta, Edmonton, Canada.

Glucagon has been reported to increase the cardiac contraction in various animal species and the dynamics of contraction resembled those of cardiac glycosides. Cardiac glycosides-induced contraction has been suggested to be associated with a shortening of the action potential duration (APD) and an inhibition of the Na⁺-K⁺-stimulated membrane ATPase. The present investigation deals with the effects of glucagon (5, 10, 20 and 50 $\mu g/ml$) and ouabain (10⁻⁷M) on the simultaneously recorded transmembrane potential and contraction; and Na⁺-K⁺-ATPase of human papillary muscles obtained from patients undergoing corrective open heart surgery. Glucagon in all concentrations increased the contraction associated with a corresponding shortening of the APD and an inhibition of the ATPase in 4 muscles obtained from patients suffering from mild heart failure. The percent increases in the contraction produced by 5, 10, 20 and 50 $\mu g/ml$ of glucagon were 15 ± 4 (S.E.), 23 ± 3.5, 42 ± 4 and 44 ± 4 respectively. Glucagon did not produce any significant change in the contraction, APD and ATPase activity in 24 muscles obtained from patients suffering from chronic heart failure. Ouabain, in all the muscles, increased the contraction associated with a corresponding shortening of the APD and an inhibition of the Na⁺-K⁺-ATPase. These results indicated that glucagon-induced positive inotropic effect might be associated with an inhibition of Na⁺-K⁺-ATPase and shortening of the APD. Also glucagon was ineffective in affecting the APD, contraction and ATPase of the muscles from patients of chronic heart failure. (Supported by AHF 5529054 and CHF).

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CEREBELLAR CONTROL OF IPSILATERAL VESTIBULAR INHIBITION OF TROCHLEAR MOTONEURONS. W.

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Ipsilateral activation of the vestibular nerve evokes a disynaptic IPSP in trochlear motoneurons with a latency of 1.3 msec which is followed by a depolarization lasting 35 msec and a second prolonged hyperpolarization. Intracellular chloride injection of these motoneurons produced a simultaneous reversal of these three potentials, demonstrating the intermediate depolarization to be produced by disinhibition. Since other experiments showed that these IPSPs are generated by neurons in the superior vestibular nucleus, the question was posed whether the cerebellum could generate this phenomenon by inhibitory control of these inhibitory neurons. Interaction of a direct floccular stimulation with an ipsilateral vestibular nerve activation produced a marked reduction in the vestibular IPSP in trochlear motoneurons. In order to discard the possibility that primary vestibular fibers activated antidromically during floccular stimulation could produce spurious results, a series of experiments was performed following chronic section of the vestibular nerve. Under these circumstances, floccular stimulation generated a similar disinhibitory depolarization in the trochlear motoneuron. This depolarization was followed by a prolonged C1- sensitive hyperpolarization, demonstrating that it is produced by a postinhibitory rebound. It is concluded that floccular Purkinje cells have a direct inhibitory action upon the inhibitory neurons of the superior vestibular nucleus.

"CENTRALLY MEDIATED CARDIOVASCULAR EFFECTS OF ANTICHOLINESTERASE"

E. Preston, Jr. and C. Heath, Dept. of Pharmacology, University of Alberta, Edmonton, Canada.

Organophosphate poisons cause hypotension by their probable disturbance of several synaptic regions in the vasomotor pathway. The following experiments test the hypothesis that cholinesterase inhibition in the medulla causes vasomotor depression. Intravenous injection of 5 $\mu g/Kg$ SOMAN* in anesthetized artificially ventilated control rabbits established that this dose is too small to have systemic effects. However when 5 $\mu g/Kg$ SOMAN was injected into the left vertebral artery, bradycardia, vasodilatation and hypotension occurred. Heart rate was restored by vagotomy and the vasodilatation-induced hypotension was reversed by intravenous atropine. Titrimetric analysis of cholinesterase activity in whole medullas confirmed that such intravertebral injections completely inhibited the enzyme. It is likely that SOMAN disturbs medullary cholinergic mechanisms involved in the control of heart rate and vasomotor output. In the latter case muscarinic reseptors are involved.

* Pinacolyl methyl phosphonofluoridate

Supported by the Defence Research of Canada

1368 CELLULAR ACTIVITIES IN EPILEPTOGENIC FOCI OF IMMATURE CORTEX. D. A. Prince and M. Gutnick.
Dept. of Neurology, Stanford Univ. Sch. of Med., Stanford, California, U.S.A.

Experiments were done on acute penicillin foci in pericruciate cortex of locally anesthetized 3-12 day-old kittens to identify characteristics of neuronal activities which might account for the decreased seizure susceptibility of immature animals. Surface interictal discharges were extremely variable in amplitude and duration; brief afterdischarges occurred rarely. No slow DC shifts were recorded in immature foci during repetitive interictal activity. Surface interictal discharges were accompanied by intracellularly recorded depolarization shifts (DSs); however, DSs and other evoked synaptic potentials in the kitten were longer in duration and more variable in amplitude than in the adult animal. Spikes were also of long duration (over 5 msec.) and repetitive spike generation rarely occurred during spontaneous activity. During DSs most neurons generated only 1-5 spikes and the spike frequency did not exceed 100/sec., even during injury discharges. The duration of IPSPs which followed DSs was not sufficient to account for the period of refractoriness for DS generation lasting 2.5 sec. or longer which followed a single epileptiform event in some foci. The data suggest that asynchrony of activities in the population, reduced capacity for repetitive high frequency spike generation and failure of excitatory synaptic electrogenesis at relatively low frequencies all contribute to the decreased seizure susceptibility of immature cortex.

THE ACTION OF 5-HYDROXYTRYPTAMINE AND CYCLIC AMP ON MEMBRANE POTENTIALS IN THE SALIVARY GLAND OF THE BLOWFLY. W.T.Prince and M.J. Berridge, A.R.C. Unit of Invertebrate Chemistry and Physiology, Dept. of Zoology, Cambridge, England and Dept. of Pharmacology, Cambridge, England.

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Secretion by the salivary gland of the blowfly (Calliphora erythrocephala) is stimulated by 5-hydroxytryptamine (5-HT). 5-HT is thought to use cyclic 3',5'-adenosine monophosphate (cyclic AMP) as a second messenger because cyclic AMP mimics the effect of 5-HT on secretory rate. The abdominal portion of the gland is a tubular structure composed of a single layer of cells and closed at one end. To gain further insight into the mode of action of 5-HT in this tissue a technique has been developed for measuring transepitheial potential and intracellular potential across either the serosal or luminal membrane. The results show that both cyclic AMP and 5-HT have their actions on potential at the luminal membrane. There is very little change at the serosal membrane. Rather surprisingly the action of cyclic AMP on the transepithelial potential is opposite to that of 5-HT. The reason for this seems to be that 5-HT has two actions. One is a direct action on anion movement whilst the other uses cyclic AMP as an intermediate and stimulates cation transport.

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VISUAL RESPONSES IN BRAIN OF GOLDFISH. C. L. Prosser, J. D. O'Benar, R. H. Peterson, and G. C. Offutt. Physiology and Biophysics, Univ. of Ill., Urbana, Illinois, USA. Visual responses were recorded as spikes from optic nerve fibers, tectal neurones and Purkinje cells, as evoked potentials from tectum and cerebellum. Most retinal axons show center-surround contrast, some are color opponent or double opponent cells. ganglion cells are directionally selective, often within receptor fields of "on" centers, some tonic, others phasic. Tectal neurones show complex fields, long latency and recovery time, also habituation. A tectal or tegmental unit may be desensitized to movement in one direction without loss of responsiveness to movement in other axes. Visual and tactile input may converge on single tectal cells and visual and auditory on tegmental cells. Periventricular pyriform neurones fire in bursts to input from contralateral tectum. Evoked potentials are negative at surface and in regions at a depth, positive in mid-layers of tectum. The deep (pyriform) negative wave is labile and may change from "on" to "off." Early negative responses may have a labile second wave (40 msec) and pairing flashes with shocks may bring in new late waves (500 msec). Visual responses in cerebellum are relayed via ipselateral tectum with one synapse. Visual field for one Purkinje cell is very large and fails to show the patterning seen for tectal neurones. No retinal projection pattern is found in cerebellum but sensitivity to stationary spots is high. Evoked potential responses in Purkinje layer is enhanced with cooling to a maximum at 16°C. Golgi and basket neurones appear less important than in cerebellum of other vertebrate classes.

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GLUCOSE DISAPPEARANCE RATE AFTER EXERCISE. E.D.R. Pruett and T. Amundsen Institute of Work Physiology, Oslo, Norway.

Glucose (0.5 g/kg body weight) was infused 15 min after the termination of exercise during a series of metabolic studies involving healthy young men in the post absorptive state, exercising on the bicycle ergometer or the motor driven treadmill at exactly measured work loads of from 20% to 90% of their maximal aerobic power (max \$\forall O_2\$). The disappearance rate of the infused glucose was different after different work loads, i.e. exercise of greater severity resulted in an increased disappearance rate. The variation in disappearance rate was not dependent upon either the total energy utilization or upon the total carbohydrate utilization during the exercise. In addition, the variations in glucose disappearance rate were found to be nearly independent of the duration of the exercise, in that exercise for as little as one minute at a given work load resulted in the same disappearance curve for the infused glucose as did exercise to exhaustion at exactly the same work load. On the other hand, the rate of disappearance of the infused glucose was found to depend upon the rate of energy utilization or of carbohydrate utilization; i.e. the severity of the exercise work load as it is related to the individual's max V_{O2} . Apparently, mechanisms which are responsible for the removal of infused glucose from the blood after exercise are activated very early in the exercise, and the magnitude of the activation is dependent upon the relative severity of the exercise.

1372 EFFECT OF ACUTE AND CHRONIC CAFFEINE ADMINISTRATION ON THE LIPID METABOLISM IN RATS. J.Pucsok, L.Szollár, J.Sós, M.Jáky. Inst.of Pathophysiology, "Semmelweis" Univ.of Med. Budapest, Hungary.

Lipid composition of the liver and serum was studied in black rats given a cardiovasopathogenic diet, (CVP Sós 65) combined with provoked hyperlipaemia induced by caffeine. The lipid content of the serum and liver was determined by method of Folch, then lipid fractions were separated by thin-layer chromatography. Fatty acid methylesters of the lipid components were studied by gas chromatography. Acute caffeine administration augmented the level of free fatty acids in serum. Chronic caffeine administration increased the quantity of triglycerides, phosphatides and free fatty acids, and there are qualitativ and statistically significant quantitativ changes of fatty acid contents of main lipid fractions. Dietary caffein increases the hyperlipidaemic effect of CVP, and its chronic administration can play a possible role in the damaging effect of cardiovasopathogenic diet.

1373 IMIDAZOLEGOXOGLUTARATE AND GASTRIC JUICE. P. Puig-Muset. J. Martín-Esteve. I. Beguiristain. P. Puig-Parellada. Res. Dept. Lab. P. E. V. Y. A. - Molins de Rey-Spain.

In the study of drugs which appear capable of regulating the 3'5'-AMP-c and Ca[†] dependent functions we experimented with Imidazole and derivatives. Male rats weighing 200 g. were used. After a fastening period of 48 h. they were submitted to pyloric ligature. The drug was given in one single 414 mg/kg. i. p. injection (equivalent to 200 mgr.free Imidazole). The animals sacrified after 5 h., the gastric juice measured, and the mucouses carefully axamined with regard to ulcerations. The H[†] concentration of the supernatants established up to pH 7, using a Titrimetric Radiometer with recorder. The results expressed as mEq H[†]. The administration of imidazole-oxoglutarate to the rats induced a decrease in the total volume of gastric juice representing 50% of that segregated by the control rats. This decrease parallels the H[†] concentration diminutions and the total acidity. In the gastric juice substantial quantities of the injected Imidazole are found. The ulceration indexes are cleary different with the values, near to zero, in the treated animals. Calcium in gastric juice and plasma, undergo significant reductions.

1374 CHEMICAL SENSITIVITY OF SINGLE CORTICAL NEURONS DURING SEIZURES. Ernie A. Puil, R.J. Reiffenstein and Cecile Triggle. Department of Pharmacology, University of Alberta, Edmonton 7, Alberta, Canada.

A knowledge of the responsiveness of single cortical cells during epileptiform after-discharges is a necessary preliminary for understanding the cause of abnormal activity in epileptic foci. In the present series of experiments, the firing pattern of neocortical neurons subjected to iontophoretic application of L-glutamic acid and/or γ-aminobutyric acid (GABA) was examined during electrically-induced seizures in cerveau isole preparations. Both glutamate and GABA exhibited their well known respective excitatory and depressant effects before and during seizures. However, periods were observed in the course of seizures where the effects of glutamate or GABA could not be detected. In addition, GABA was found on occasion to provoke firing and to increase spike amplitude. Similarly glutamate was capable, at times, of decreasing neuronal firing and spike amplitude. These findings are interpreted as being a reflection of synaptic input during the afterdischarge. Thus the data suggest that a strong depolarization and inactivation of cells may occur during an afterdischarge and provide presumptive evidence that excessive excitatory synaptic drive may play a role in the maintenance of seizures.

Supported by the Medical Research Council of Canada.

DISTRIBUTION OF CORTICAL EVOKED POTENTIALS TO SCIATIC STIMULATION IN RATS; J.Pusztai and E.Kuzmann. Department of Comp. Physiology, Eötvös Lóránd University, Budapest, Hungary.

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Authors recorded the distribution of somatosensory evoked responses on the cortical surface by applying sciatic electric shocks in acute experiments. On the basis of the data the map of the somatic sensory representation areas has been constructed. The distribution of the sciatic evoked potentials, similarly to the topography in other laboratory animals shows two foci of punctum maximum. The variability of the primary responses has been estimated by the statistical evaluation of the localization of the averaged evoked potentials.

CALCIUM INDEPENDENCE OF ACETYLCHOLINE SECRETION AT THE NEUROMUSCULAR JUNCTION. D.M.J. Quastel, J.T. Hackett, and J.D. Cooke. Dept. of Pharmacology, University of British Columbia, Vancouver, B.C., and Dept. of Physiology, Dalhousie University, Halifax, N.S., Canada.

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A multiplication of the spontaneous frequency of miniature end-plate potentials (F) in rat or mouse diaphragm can be produced by: 1) depolarization of the motor nerve terminal; 2) raised osmotic pressure and 3) a variety of central depressant drugs including ethanol, chlorpromazine and barbiturates. Only the response to presynaptic depolarization is inhibited by calcium depletion (no Ca, 10 mM EGTA). Over a wide range F is exponentially related to osmotic pressure, ethanol concentration, or degree of depolarization (Ca present). In each case this relation can be explained on the basis of a progressive reduction of an energy barrier which normally limits quantal release, and a power relation between release and external Ca concentration also follows. Ethanol multiplies Ca-dependent depolarization-evoked release to the same extent as it multiplies Ca-independent spontaneous release. This result implies that both kinds of transmitter section share a final common pathway which requires little or no Ca. Hence, the role of Ca is confined to coupling secretion to presynaptic depolarization. — This work was supported by the Muscular Dystrophy Association of Canada.

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RESISTANCE IN THE DOG. D. Radawski, J. Scott, R. Daugherty, Jr., J. Dabney, and F. Haddy. Dept. of Physiol., Michigan State University, East Lansing, Michigan 48823 U.S.A.

We have shown that severe local hypercapnia lowers vascular resistance in the dog fore-limb, heart, and kidney (Am. J. Physiol. 213:1102, 1967). We now report the effects of graded, local changes in CO2 on total (Rt) and segmental resistances in skin and muscle and the effect of severe hypercapnia on forelimb weight. Arterial blood was pumped through an isolated donor dog lung at a constant rate into the brachial artery of a collateral-free forelimb (n=10). The isolated lung was sequentially ventilated with room air, 20% O2-5% CO2, 20% O2-75% CO2, 20% O2-10% CO2, 20% O2-15% CO2, 20% O2-20% CO2. Corresponding pH values of forelimb venous blood were 7.64, 7.32, 7.22, 7.15, 7.02, 6.91. Changing venous pH from 7.64 to 7.32 produced a fall in perfusion pressure (Pp) from 146 to 122 mmHg. This fall in Rt was due mostly to a fall in skin small vessel resistance. Further stepwise decreases in venous pH to 6.91 produced progressive falls in Pp to 101 mmHg, again due mainly to a fall in skin small vessel resistance. There was also a small decrease in skin venous resistance and a small shift of blood flow from muscle to skin. Muscle resistances were not regularly affected. Ventilation for 30 min with 20% O2-20% CO2 did not affect forelimb weight. These studies fail to indicate that severe prolonged hypercapnia alters vascular permeability to protein. They also show that graded, local increases in CO2 actively dilate skin small vessels and perhaps skin veins. Since muscle small vessel resistance remained unchanged while transmural pressure fell, increases in CO2 tension probably also relax vascular smooth muscle in this segment.

EFFECTS OF LOCAL CHANGES IN CO2 ON FORELIMB WEIGHT AND SKIN AND MUSCLE SEGMENTAL VASCULAR

ON THE CHARACTER OF THE BIOELECTRICAL ACTIVITY OF THE COMPLEX STOMACH. T.Radev, M.Panasova, I.Stojanov, F.Atanasova, Tz.Georgiev. Inst. of Comparative Pathology of Animals
and Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Groups of spik potentials without slow waves are recorded from the reticulum, dorsal and ventral sacs of the rumen, their caudal blind sacs and the left longitudinal pillar. These groups correspond to the movements of the reticulo-ruminal cycle. Slow waves were recorded from the abomasum (6 to 7 cycles/min). Immediately after the reticulo-ruminal cycle there appeared spike potentials after the slow potentials from the abomasum and duodenum. Novokain blokade of the cervical vago-sympathetic nerves as well as atropin provoked disappearance of the reticulo-ruminal cycle, but had no effect on the slow potentials from the abomasum and duodenum. The reticulo-ruminal cycle disappeared after cholinergic drugs and groups of spike potentials occurred in the rhythm of slow potentials of the abomasum.

THE EFFECT OF PROSTAGLANDIN E₁ ON THE PERISTALTIC REFLEX OF THE ISOLATED GUINEA-PIG ILEUM. B.Z.Radmanović. Dept.of Pharmacology, Med.Faculty, Beograd, Yugoslavia.

The effect of prostaglandin E_1 (PGE $_1$) on the peristaltic reflex of the isolated guinea-pig ileum was investigated using Trendelenburg's method. When the peristaltic reflex was elicited by constant subliminal intraluminal pressure, PGE $_1$ in small concentrations (5-10 µg/ml) first potentiated peristalsis, and after that inhibition occured. Higher concentrations (0.1-0.5 µg/ml) produced contracture of longitudinal and circular smooth muscles and long-lasting block of the spontaneous peristaltic waves. The same effect of PGE $_1$ was seen when peristaltic reflex was elicited by raising intraluminal pressure for 3-5 cm $_1$ 0 intermittently (every 10 min for 90 sec). Larger doses of PGE $_1$ (0.5 and 1.0 µg/ml) prologned the block of peristalsis caused by adrenaline. On the other hand, on the reserpinized guinea-pig ileum, PGE $_1$ in larger doses caused only short-lasting abolition of peristaltic reflex.

A MODEL OF CONTINUOUS ACTIVITY MONITOR FOR SMALL LABORATORY ANIMALS.

R. Radomirov, J. Lucanov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

It is well known that the movements provoke displacement of the center of gravity of the body. The proposed model provides the possibility of controlling the motor activity of small laboratory animals on the basis of this principle. A disc with a cone in the center of its lower side, placed on another disc, alters its equilibrium under the action of a load outside the point of contact between the two radii. Contact springs on the opposite surfaces of both discs generate electrical impulses upon any displacement of the upper disc and this provides the opportunity of estimating the changes occurring in the center of gravity of a body placed on the disc. This device could operate continuously (more than 24 hr). The number of displacements of the center of gravity during the experiment is calculated by an electromagnetic counter. By an electronic integrator the electrical impulses could be transferred to a recording apparatus. The latter yields information on the motor activity of the animal.

AN EXPERIMENTAL MODEL TO DISSOCIATE THE H-ION SECRETION IN THE PROXIMAL RENAL TUBULE FROM CARBONIC ANHYDRASE ACTIVITY. H.W. Radtke, G. Rumrich, S. Klös, K.J. Ullrich. Max-Planck-Institut für Biophysik, Frankfurt/M., Germany.

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Proximal fluid reabsorption, measured with the Gertz shrinking droplet method, increases linearly with increasing HCO₃-concentration in the capillary perfusate up to 30 mM. When perfused with a bicarbonate-free phosphate-buffered salt solution a "basic" reabsorption of about 20% of control remained. This "basic" reabsorption can be partially blocked by acetazolamide (10⁻⁴M), which indicates that it is due to endogenously produced CO₂-HCO₃. The lipid soluble glycodiazine-buffer (30 mM) and, to a lesser extent, also the sulfamerazine buffer, can replace the bicarbonate buffer in promoting proximal isotonic reabsorption. Acetazolamide (10⁻⁴M) reduces the reabsorption in glycodiazine buffered perfusions by about 20%, which is equivalent to blockade of the effect exerted by endogenously produced CO₂-HCO₃. From these data it can be deduced that the proximal H* secretion can be studied independent of carbonic anhydrase (CA) function by perfusing the capillaries with glycodiazine buffered solution also containing a potent CA-inhibitor. Furosemide (10⁻⁴M) inhibits the proximal fluid reabsorption in a bicarbonate containing as well as in a glycodiazine buffered system (where the endogen CO₂-HCO₃ production is present) by 50% of the corresponding acetazolamide inhibition. This indicates that furosemide exerts a CA-inhibiting effect on the proximal convolution only and not a chloruretic effect.

THE KININFORMING SYSTEM IN THE UNSPECIFIC REACTION. M.Rădulescu, I.Baciu, L.Grosu. Dept.of Physiology, Inst.of Med. and Pharm.Cluj, Romania.

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The changes of the kininforming system (K.S.) in 20 dogs in vigil exposed to hypobaric hypoxia equalling altitudes of 5500 m or 6500 m have been studied. Before hypoxia and at different intervals the kininogen (K-gen) and the plasmakinins (Pl-k) have been determined. The 5500 m hypoxia produces an important decrease of the K-gen and Pl-k concentration at 2 hrs exposure and an increase of both parameters at 4 hrs. The continous exposure to 8 and 12 hrs does not significantly modify the K-gen and Pl-k behaviour. The normal concentration of the K.S. factors is restablished by removal of the hypoxic stimulus. The 6500 m hypoxia elicits an increase of the K-gen level at 2 hr exposure and a decrease of Pl-k release. At 4 hrs exposure the K-gen and Pl-k concentration tends to normalise. Repeated exposure to the hypoxia of 6500 m during 5 days produces a progressive reduction of the response capacity of the K.S. in isolated hypoxic stresses as well as an increase of the initial K-gen values along with a decrease of Pl-k beginning at the third day.

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INVESTIGATIONS ON SINGLE UNITS OF HUMAN BRAIN DURING ONE-STAGE STEREOTAXIC OPERATIONS. S.Raeva, A.Kadin, A.Konovalov, V.Seliverstov, T.Merschikova. Dept.of Memory Problems, Biological Center, USSR Acad. Sci., Puscino on Oka, and Inst.of Neurosurgery, USSR Acad. Med.Sci., Moscow, USSR.

The activity of 400 units of certain deep cerebral structures was studied in man with tungsten microelectrodes with tip diameter of 1-2 microns and resistance of 1-10 meghom. The investigation of peculiarities of spontaneous and evoked unit activity has permitted the specification of the individual boundaries of conducting and nuclear structures, the detection of the precise structural funcitonal differences of the thalamus, globus palladium, caudate nucleus and other deep structures and the identification of some zones inside the same cellular area. Burst type rhythmical activity of units recorded from deep structures was correlated in frequency with the tremor and was very responsive to afferent stimuli. Quantitative analysis of these units has shown different features of their functioning in different deep structures. The data obtained permitted the analysis of the neuronal peculiarities of the structural functional organization of the investigated structures and revealed some central links of the system involved in the mechanism of parkinsonian tremor.

DENDRITIC SPINES AND SYNAPTIC POTENCY EXPLORED THEORETICALLY. W. Rall and J. Rinzel. National Institutes of Health, Bethesda, Maryland, USA.

We wished to compute the effects of synaptic input received by a dendritic spine, and to examine possible functional implications of changes in spine stem resistance. We used an idealized neuron model composed of several dendritic trees; the branching satisfied the constraint (on 3/2 power of branch diameter) that permits mathematical transformation between a tree and an equivalent cylinder. Passive nerve membrane was assumed; symmetric branching was useful (but not necessary) for superposition of boundary value problems. Rigorous mathematical solutions (steady state and transient) were obtained for current injection at a single dendritic branch. These solutions were coupled computationally with a spine model whose spine-head membrane received synaptic excitatory conductance input. Results computed for a wide range of stem resistance and dendritic input resistance will be illustrated. Over a favorable range, a decrease (increase) of stem resistance causes a significant increase (decrease) in the dendritic EPSP and its contribution to the somatic EPSP. We suggest that fine adjustments of the stem resistances of many spines could provide one way for an organism to adjust the relative weights of the many synaptic inputs to each neuron, thus providing a possible contribution to plasticity and learning. Also, the anatomical fact that finer spine stems occur preferentially on finer and more distal dendritic branches seems to agree with a theoretical notion of an optimal range for the ratio of spine stem resistance to dendritic input resistance.

DIFFERENCES AT SENSIBILITY TO BARBITURATE RELATED TO ESTROUS CYCLE AND SE-XUAL HORMONES IN RATS. <u>A.Ramos., D.Ajami., B.Pardey., F.J.Hernández</u>. Dept of Biochemical, Bioanalisis Shool. U.C.V. Caracas, Venezuela.

Electrocorticographic recordings have been made in 1)Normal female adult Sprague-Dawley rats kept in a light control room and with regular estrous cycle. 2)Animals at the 14th day of pregnancy.3)Rats with ovariectomy and 4)Rats submitted to systemic administration of Estradiol Benzoate(0.5 microgr.) and Progesterone (0.5 miligr.). We have observed a greater sensibility to barbiturate during Proestrous and in castrated rats receiving Progesterone (0.5 mg/10 days). The 14th day of pregnancy we have observed a greater resistance to barbiturate. We consider that the differences of sensibility to barbiturate observed in ours experiments may be related to the relative concentration of estrogen/progesterone and the progesterone/20 alfa-OH progesterone.

DIFFERENTIAL DISTRIBUTION OF AUTONOMIC NERVES TO THE HEART. W.C. Randall, J.A. Armour, W.P. Geis. Dept. of Physiology, Loyola Univ. Med. Ctr., Maywood, Illinois, U.S.A. 1386 In contrast to conventional views of cardiac autonomic outflows, a concept of localized innervation of specific portions of the heart is emerging. Distribution of nerves to discrete epicardial segments is well documented. Papillary muscle and interventricular septal (IVS) contraction have been demonstrated in vivo and their contractile force is greatly augmented under positive inotropic drive (stellate stimulation, administration of iso-proterenol, norepinephrine). The papillary muscles possess discrete innervation, and electrical stimulation of small cardiac nerves induces differential inotropic actions. Thus, the posterior papillary muscle of LV receives its primary sympathetic innervation from the left whereas its anterior counterpart is supplied by both left and right sympathetics. Both muscles show inhibition during vagal stimulation. Contractile force as well as intramyocardial pressure recordings indicate the right endocardial musculature of IVS performs as a functional portion of RV while the left portion follows LV. Apical portions of IVS appear to be innervated by sources different from those which supply basal portions. Epicardial musculature is supplied by a superficial plexus less than 0.25 mm below the surface, emanating from nerve projections onto the atria, along the pulmonary artery, and from the coronary plexuses. Endocardial surfaces receive important innervation via projections along the pulmonary artery and interatrial septum as well as from large nerves located at the junction of the inferior vena cava and the inferior border of the left atrium. (Supported by Grant HE 08682 of the NIH, USPHS).

EFFECTS OF IODOACETIC ACID ON CONTRACTILITY AND ION MOVEMENTS IN RAT MYOMETRIUM. P.K. Rangachari, D.M. Paton and E.E. Daniel, Dept. of Pharmacology, Univ. of Alberta, Edmonton 7, Alberta, Canada.

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The aim of this study was to determine the role of glycolysis in spontaneous contractility and ion movements in rat myometrium. For this purpose the effects of iodoacetic àcid (IAA) on the recovery of tissues from Na⁺-enrichment were studied. Addition of 4.6 mM K⁺ to Na⁺-rich tissues resulted in Na⁺ extrusion, K⁺ accumulation and onset of contractility. IAA (0.2-0.5 mM for 30 min) inhibited these changes and, in addition, caused swelling due to a gain of Na⁺ and H₂0. Addition of pyruvate (25 mM) to IAA-treated tissue produced a coupled Na⁺ extrusion and K⁺ accumulation and a reduction in swelling but contractility did not recover. The coupled movements of Na⁺ and K⁺ produced by the addition of pyruvate to IAA-treated tissues were prevented by ouabain (1 mM) or anoxia. These effects of pyruvate on IAA-treated tissues were also produced by succinate and β -hydroxybutyrate. Failure of contractility to recover after the addition of pyruvate to IAA-treated tissues was not due to insufficient tissue K⁺ but may reflect either a direct action of IAA on contractility or a lower energy requirement for ion movements. These studies have shown the importance of glycolysis for the maintenance of ion movements and contractility in rat myometrium; that oxidative phosphorylation alone can provide the energy for ion movements; provided evidence for a second Na⁺ extrusion mechanism. (Supported by grants and fellowships from the Medical Research Council of Canada and the Alberta Heart Foundation).

CROSS-FLOW IN THE SHEEP PLACENTA. J.H.G.Rankin. Dept.of Physiology, University of Colorado Medical Center, Denver, Colorado, USA.

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Recent anatomical studies and observations on the effect of reversing one of the flows have indicated that the sheep placenta should exhibit the characteristics of a cross-flow exchanger. The cross-flow exchanger is presented in the placental literature as having operating characteristics similar to those of a counter-flow exchanger. The sheep placenta has been shown to resemble a parallel-flow (concurrent) exchanger when exchange is "flow limited," and the existence of cross-flow in this placenta has therefore been rejected. The cross-flow exchanger only resembles a counter-flow exchanger when there is no mixing across the diameter of the tubes. When such mixing occurs, as should be the case in the capillaries of the sheep placenta, and the exchange is "flow limited," the cross-flow exchanger acts like a parallel-flow exchanger. The presence of cross-flow in the sheep placenta is therefore compatible with the available data. A cross-flow exchanger of this type exhibits anomalous patterns of exchange. When the flows are equal the effectiveness of exchange is equal to $d(1-e^{-d})/(2d+e^{-d}-1)$ where d is the permeability divided by one of the flows. It can be seen that when d is 3 the effectiveness of exchange is 13% greater than the effectiveness of exchange when d is greater than 10. Substances to which the placenta is very permeable would thus be exchanged less effectively than substances to which the placenta is relatively impermeable.

EFFECTS ON INSULIN OUTPUT AND ON BLOOD FLOW, OF INSULIN INFUSION INTO AN ISOLATED PORTION OF PANCREAS IN SITU. A.M. Rappaport, S. Ohira, J.A. Coddling, G. Empey, and R.E. Haist. Dept. of Physiology, Univ. of Toronto, Toronto, Canada.

1389

Eight dogs had the vessels of the body and uncinate process of the pancreas severed (and this part of the pancreas isolated) except for the inferior pancreatico-duodenal artery. The remaining or splenic portion of the pancreas was left intact and in place. Doses from 200 $\mu\rm U$ to 8 mU/min. of commercial insulin were infused into the inferior pancreatic artery via its duodenal branch. The infused insulin together with the endogenous insulin were continuously recovered in the blood drained from the superior pancreatico-duodenal vein. The plasma glucose level was maintained practically unchanged by the insulin released from the splenic portion of the pancreas The steady glucose level during the infusion into the isolated portion of the pancreas demonstrated its complete isolation as well as the total recovery of the insulin delivered to it. The infusion of various doses of insulin into the inferior pancreatic artery regularly and significantly decreased the output of insulin from the isolated pancreas. The decrease ranged between 40 to 80% of the pre-infusion values.

ACTION OF RETIGULAR FORMATION ELECTROTONIZATION ON BRAIN BIOELECTRIC ACTIVITY AND THE PERIPHERAL MOTOR SYSTEM. V.Räscanu, C.Solomon and C.Bälteanu. Institute for Public Health and Medical Researches, Jassy, ROMANIA.

Evoked motor potentials, cortical response to intermittent light stimulation (ILS) and direct and reflex excitability of the peripheral motor system during electrotonization of the RF were investigated in rabbits. EEG recorded from neocortex, rhinencephalon and midbrain RF showed that during RF electrotonization the fundamental and synchronized basal rhythn obvious in the partieto-occipital motor cortex and thalamus turns into an arrousal type of activation, with increased cortical reactivity to ILS and evoked motor response, and peripherally in a hypoexcitability and of the reflex summation curves. During RF catelectrotonization there were slow irregular waves - irregular amplitude in the cortex and subcortex, - less evident in the RF, where rapid rhythms prevailed. A decreased cortical reactivity to ILS and a rise in stimulation threshold if evoked motor potentials were also noted. Peripherally, increased direct excitability and a decreased spinal reflex electroactivity were noted. Within 3-lo sec after cessation of the action of the electrotonizing current on RF, EEG and the bicelectric reactivity of the peripheral motor system were of opposite sense to the electrotonizing current applied, then gradually returned to normal values.

1391 EFFECT OF IRRADIATION ON STEROID METABOLISM. S.K. Rathi. Dept.Zoology, Govt. Post-Graduate College, Kota, India.

Male and female Indian catfish, <u>Heteropneustes fossilis</u> were treated with various sex steroids and then subjected to irradiation. The role of steroid was recorded using various parameters such as gonadosomatic index, mortality rate, changes in the weight of gonads, histological and histochemical alterations in the gonadal cells. Estrogen produced deleterious effects on the developing eggs. Irradiation also produced degenerative changes. But when both treatments were given simultaneously, the damaging effect was reduced considerably. This was attributed to increased androgen production following irradiation. However, estrogen produced degenerating effects on the testes. But when treatment was carried out with irradiation, damaging effect was accelerated. Hence, estrogen acted as a radiosensitizing agent in male gonads. Testosterone propionate accelerates spermatogenesis in males but when this experiment was carried out with irradiation, degenerative changes were observed. This steroid also acted as a radiosensitizing agent. In females T.P. produced degenerative changes which were accelerated when treatment was carried out with internal irradiation. All these experiments indicate that in males, steroid hormones act as a radiosensitizing agent whereas their mechanism in females is quite different.

1392 CARDIAC OUTPUT AND O₂ UPTAKE AT ONSET OF EXERCISE. J. Raynaud, Ph. David, A. Lockhart, J. Durand. C.C.M.L. 129, rue de Tolbiac, (75) Paris, FRANCE.

The phasic relationship between systemic blood flow (Q) and O_2 uptake (VO2) prior to the steady state exercise (st.st.ex.) has been studied in 10 subjects during right heart catheterization (VO2 st.st.ex.=1 l/mn). Q was measured by constant infusion of 85 Kr, O_2 contents of pulmonary ($C\bar{v}_{O2}$) and brachial (Ca_{O2}) arteries by the Van Slyke manometric technique and VO_2 was computed as the product: $\dot{Q}(Ca_{O2}-C\bar{v}_{O2})$. These measurements were made at intervals of 15 sec during the 1st mn and of 30 sec until the 4th mn. At the 40th sec, 70 % of the maximal increase in \dot{Q} is achieved but only 43 % of st. st. \dot{V}_{O2} . The unchanged Ca_{O2} and the abrupt increase in \dot{Q} result in a steep rise in O_2 transport to the tissues ($Q.Ca_{O2}$). As regards $C\bar{v}_{O2}$, it decreases slowly so that the increase of ($Ca_{O2}-C\bar{v}_{O2}$) lags behind that of \dot{Q} . But at the end of the 2^{nd} mn of ex.both \dot{Q} and $(Ca_{O2}-C\bar{v}_{O2})$ have reached st.st. values. Hence O_2 flow returning to the lungs ($\dot{Q}.C\bar{v}_{O2}$) at onset of exercise is transiently higher than at rest or at st.st., indicating that the increased O_2 availability is not accompanied by an equal utilization by the tissues. This response may reflect either an inadequate adjustement of muscular perfusion with regard to metabolism or a lag in the utilization of O_2 by the oxydative enzymatic systems in the working muscles or, more likely, a transfert of blood from the peripheral vascular beds.

IS OUR VISUAL SYSTEM BILINGUAL? J.P. Raynauld Centre des Sciences Neurologiques, Université de Montréal, Montréal, Canada.

1393

An invariant representation of the shape of object occurs in the visual cortex regardless of whether the optic nerve fibres carry spike patterns coded by the rod and the cone system in the retina. Since the spike patterns are different in the two cases how does the brain maintain this shape invariance? In the auditory system such an invariance occurs through a learning process, The spoken words "femme" and "woman" generate two different patterns of spike activity in the auditory nerve, yet there is an invariance of representation for persons who understand french and english. In the goldfish retina, a very close association was found between the rod system and the red cone system. During a light adaptation study, on-centre cells in the dark became red on-centre cells after light adaptation; offcentre cells similarly turned out red off-centre cells after light adaptation. On an a priori basis, the rod system has a 50-50 chance of association with the red or the green cone system (neglecting the blue cones). These findings suggest that the association of the red cone system with the rod system may be the key to the shape invariance in the visual system.

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INTERACTION BETWEEN Ca⁺⁺, TETRODOTOXIN AND CIGUATOXIN IN CONTROL OF MEMBRANE SODIUM PERMEABILITY. M.D. Rayner and T.I. Kosaki. Department of Physiology, School of Medicine, University of Hawaii, Honolulu, Hawaii, U.S.A.

The dose-response curve for effect of ciguatoxin (CT) on frog muscle membrane potentials indicates a sharp depolarization from normal resting potential to 40-50 mV (at 20°C) in response to CT concentrations greater than $8\text{xl}0^{-8}\text{g/ml}$ (ED50 = $4\text{xl}0^{-8}\text{g/ml}$); further increase does not reduce the resting potential below 40 mV. That this depolarization is a consequence of increased Na+ permeability is suggested by the lack of effect of CT in Na-free ringer, by the prevention of CT depolarization in 10^{-6}M/ml Tetrodotoxin (TTX) and by the results of direct measurements of Na-flux in the presence of CT. When the Ca⁺⁺ concentration of the ringer is increased from 1 mM to 10 mM, the dose-response curve for CT is shifted to the right but the maximum depolarization is not altered (ED50 increases to $2 \times 10^{-7}\text{g}$ in 7.3 mM Ca⁺⁺ and to $3 \times 10^{-6}\text{g}$ in 10 mM Ca⁺⁺). Similarly, although TTX concentrations below $1 \times 10^{-8}\text{M}$ do not appreciably affect the ED50 for CT, increasing TTX from 1×10^{-8} to 1×10^{-7} increases the ED50 to $2 \times 10^{-6}\text{g}$.

1395

EFFECTS OF MALEIC ANHYDRIDE ON ION PERMEABILITY IN RED BLOOD CELLS. A.F. Rega, A.L. Obaid and P.J. Garrahan, Dept. de Química Biológica, Fac. de Farmacia y Bioquímica, Univ. de Buenos Aires. Argentina.

Maleic anhydride is a reagent which specifically combines with amino groups reversing their charge. Treatment of human red cells with this reagent results in a ten-fold decrease in anion permeability as judged by SO₄ fluxes. Tis effect is associated with an up to one hundred-fold increase in potassium permeability. The effect of the reagent on sodium permeability is comparatively less than that on potassium permeability. These results are consistent with the idea that possitive charges from membrane amino groups play a role in the ionic selectivity of the red cell membrane. Treatment of red cells with maleic anhydride also results in a progressive hemolysis which does not seem to be colloid-osmotic in nature, suggesting that amino groups are necessary for the normal stability of the cell membrane. (Supported by the Consejo Nacional de Investigaciones Científicas y Técnicas, Argentina).

NEUTRAL CARRIER MECHANISM FOR C1 -HC03 TRANSPORT ACROSS LIMITING CELLULAR MEMBRANES.
W. S. Rehm and S. S. Sanders. Dept. of Physiology. Univ. of Alabama in Birmingham, USA.

The stomach, red blood cells and other tissues possess a mechanism for the exchange of anions, particularly Cl⁻ and HCO₃⁻ between their cells and the outside medium. It is generally assumed that the exchange occurs through anion permeable channels possessing a high conductance, the driving forces being the electrochemical gradients. Work on the in vitro gastric mucosa of the frog showed that the transmucosal resistance is markedly increased by addition of Ba⁺⁺ (0.5 mM) to the nutrient (submucosal) fluid while the H⁺ rate continues indefinitely at a high level. The elevated resistance is rapidly lowered to normal levels (<1 min) by elevation of the K⁺ of the nutrient fluid (from 4 to 80 mM), with the Ba⁺⁺ still present, indicating that the site of the resistance increase is the nutrient facing membrane. The amount of Cl⁻ present in the mucosal cells is sufficient for only about 10 min of secretion, and since the elevated resistance and H⁺ rate continue for hours, Cl⁻ must enter and HCO₃⁻ leave the gastric cells at a rate essentially equal to the H⁺ rate. If the movement of Cl⁻ and HCO₃⁻ is only via conductance channels (or channel) the transport rates for Cl⁻ and HCO₃⁻ (with Ba⁺⁺-induced high resistance) could be only a small fraction of their actual rates. Hence there must be a neutral (carrier) mechanism for the exchange. Another line of attack, the effect of changes in ionic composition of the nutrient medium on the transmucosal PD, also leads to the same conclusion. (NIH and NSF support.)

1397 SAMPLING OF ALVEOLAR LIQUID FROM ALVEOLAR SURFACE BY MICROPUNCTURE.

R. Reifenrath. Max-Planck-Institute for Experimental Medicine, Department of Physiology, Göttingen, German.Fed.Rep.

The judgement of chemical and physico-chemical properties of Lung Alveolar Surfactant (LAS) generally is based on material obtained by lung washing. Therefore the question exists to what extend this material is contaminated by substances derived from bronchies, lung tissue or lung capillaries. To clarify this question a method was developed which permits (under microscopical observation) to obtain liquid from alveolar-surface of isolated, inflated rat lungs by micropuncture. A qualitative and quantitative analysis of protein by microdisc-electrophoresis shows, that the concentration of albumin in the punctured liquid is less than 20 % of the albumin-concentration in serum. We assume that the punctured liquid is contaminated by serum proteins. We expect that LAS would be free of serum proteins after improvement of the technique of puncture.

CENTRAL VENOUS PRESSURE, ARTERIAL PRESSURE AND HEART RATE DURING ACUTE BLOOD VOLUME CHANGES IN RATS. H.-W.Reinhardt, E.Hennings, M.Goepel and G.Kaczmarczyk. Div.of Exp.Anaesth.-Inst.of Anaesth., Klinikum Westend, Free University of Berlin, Germany.

Experiments were performed on well hydrated, spontaneously breathing Wistar rats under halothane anaesthesia. Two experimental sets of stepwise blood volume changes (1-25% of total blood volume during one minute) were done: 1. withdrawal followed by re-transfusion; 2. transfusion (from a donor rat) followed by withdrawal. Under these conditions the compliance of the venous system remained constant (0.4 ± 0.1 ml/cm H2O · 100 g BW). Decrease of central venous pressure was closely correlated to decrease of arterial pressure, whereas increase of central venous pressure was not. There were no significant changes of heart rate. These results indicate the lack of rapid reaction in the venous and arterial system of the rat. Obviously, a decrease of central venous pressure is followed by a decrease in cardiac output which cannot be compensated by an increase of heart rate. This inability is not due to anaesthesia; it also could be demonstrated in conscious rats.

EFFECT OF FETAL HYPOXIA ON REGIONAL CEREBRAL BLOOD FLOW. M. Reivich, A.W. Brann, Jr., H. Shapiro and R.E. Myers. Dept. of Neurology, Univ. of Penna., Philadelphia, Penna.,

1399

Prolonged partial asphyxia in the term monkey fetus produces a pattern of neuropathological change very similar to that which is seen in perinatal brain damage in the term human infant (Myers. Neurol. 19:1177, 1969). To further elucidate the underlying factors responsible for these pathological changes studies of regional cerebral blood flow (rCBF), using the Cl4-antipyrine autoradiographic technique, were performed in utero in term monkey fetuses. Four-control animals were studied as well as four animals in whom hypoxia was produced for periods of 1.6 to 3.7 hours by reducing the maternal inspired oxygen concentration to 12-14%. Fetal arterial (right brachial) Po₂, Pco₂ and pll were measured. In the control animals these values were 28.8 \pm 1.3 mm Hg, 48.3 \pm 3.5 mm Hg, and 7.30 \pm 0.02 respectively. In the experimental animals varying degrees of acidosis, hypoxia, and hypercarbia were produced. Reductions in rCBF were seen in all four experimental animals and varied from mild to severe. These changes in flow correlated very well with the duration of acidosis experienced. In addition, a distinctive pattern of flow changes was observed which was interpreted as being best explained by preferential arterial compression. The pattern of impaired flow correlates well with the pathologic pattern seen in neonatal asphyxia which strongly suggests that impaired rCBF is the direct cause of the pathological lesions.

STUDIES ON THE EFFECT OF CORTISOL THERAPY UPON THE INSULIN RESPONSE TO HYPERGLYCAEMIA IN THE THYROIDECTOMIZED DOG. A.Renauld, R.C.Sverdlik and V.G.Foglia. Inst. Fisiologia, Fac. Med., Univ. Buenos Aires, Buenos Aires, Argentina.

1400

Since a mild decrease in corticosteroid secretion is known to be associated with the hypothyroid condition, we have studied the effect of the chronic cortisol treatment on the "in vivo" insulin response to both an oral and an intravenous glucose load. Either blood sugar or serum IRI levels remained unchanged by thyroidectomy; they both increased after therapy; Conard's k constant remained unaffected after thyroidectomy (with or without cortisol therapy); the insulin response to i.v. induced hyperglycaemia was overnormal in the thyroidectomized dog and still rose after cortisoltreatment. The hypothyroid condition induced a delay for blood sugar to increase and then to decrease during the OGTT; this was corrected by cortisol therapy. The insulin response to oral glucose load was strikingly overnormal in thyroidectomized dogs and was normalized by cortisol therapy.

EXPERIMENTAL DIABETES AND SOME ASPECTS OF NERVOUS ACTIVITY IN RATS.

M.A.Requena., E. Vallecalle., R.Gómez. Dept. Physiology, Vargas Med. Sch., U.C.

V., Caracas, Venezuela.

1401

In these experiments we have looked for posible functional modifications in peripheral and central nervous system of Sprague-Dawley adult rats with experimental diabetes (Partial and total pancreatectomy; Alloxan) without treatment (glicemia above 2 gr. %°) or treated with insuline (2-4 U.). Using oscilloscopic methods we have determined the conduction velocity in the sciatic nerve in vivo and in vitro, in the motor and sensitive fibres. Through chronic electrodes we have recorded spontaneous and evoked activity in the sensorimotor cortex for more than one month. The conduction velocity in vivo and in vitro, in motor and sensitive fibres of normal animals was 54.4 mt/seg² 2.39. In animals with chronic hyperglicemia by pancreatectomy or alloxan administration there is a significant reduction of velocity but no difference between the sensitive and motor fibres. Insuline treatment does not affect the changes of velocity produced by experimental diabetes. The reduced velocity can be related to a diabetic neuropathy in accord with anatomical observations. In untreated animals we have observed low frecuency of the £CoG, increased latency of the evoked potential and low amplitude of the surface negative wave possibly related to metabolic factors.

THE MECHANISM OF ALL-OR-NOTHING REPOLARIZATION IN VENTRICULAR MYOCARDIAL FIBRES. H. Reuter & G.W. Beeler, Jr., Dept. of Pharmacol., Univ. of Berne, Switzerland, and Dept. of Physiol. & Biophys. Mayo Clinic, Rochester, Minn., USA.

Action potentials (AP) of cardiac muscle can be terminated regeneratively by the application of hyperpolarizing inward current during the plateau phase. Although certain predictions about the mechanism of this all-or-nothing repolarization (A-NR) arise from the Hodgkin-Huxley theory, the data obtained so far did not allow a generally acceptable interpretation of the phenomenon (cf. D. Noble, Physiol. Rev. 46, 42 (1966)). Our recent computational reconstruction of ventricular AP was based on the ionic currents measured by different groups utilizing the voltage clamp method in cardiac muscle. The reconstruction model predicted that A-NR occurs at any given potential as a function of time necessary for deactivation of the slow calcium inward current (I_{in}) activated during the plateau of the AP. This prediction was checked experimentally and the results agreed clearly with the AP model in showing that 1) A-NR is potential- and time-dependent, 2) at a given potential regenerative repolarization occurs if I_{in} has sufficiently decayed to be overcome by outward current ($I_{in} < I_{out}$), and 3) the threshold for A-NR decreases in the course of the AP because I_{in} is inactivated and I_{out} is activated during the plateau.

MONOSODIUM GLUTAMATE: ABSENCE OF HYPOTHALAMIC LESIONS AFTER INGESTION BY NEWBORN PRIMATES.

W. A. Reynolds, Ph. D., Naomi Lemkey-Johnston, Ph. D., L. J. Filer, Jr., M. D., Ph. D., and R.M. Pitkin, M.D. Dept. of Anatomy, University of Illinois at the Medical Center, Illinois State Pediatric Institute, Chicago, Illinois, and Depts of Pediatrics and Obstetrics and Gynecology, University Hospitals, Iowa City, Iowa, U.S.A.

Hypothalamic lesions have been reported for newborn rodents, and in a single instance, the monkey, following the injection or oral administration of large doses of monosodium glutamate (MSG). Because of the disquieting implications for the human infant whose diet may contain MSG, a search was begun on newborn macaques for hypothalamic lesions resulting from the ingestion of MSG. After fasting for 4 hours, a 50% solution of MSG was administered by stomach tube at dose levels of 1, 2, and 4 gm/kg. Sixteen newborns of two macaque species (Macaca mulatta and Macaca iris) ranging in age from 15 minutes to 14 days were treated while five infants served as controls. Six hours after MSG administration, the brains of the infants were perfused and prepared either for electron or light microscopy. No morphological differences were observed between the hypothalamic areas of normal neonatal monkeys and those ingesting MSG. Cells of the arcuate-periventricular area were normal in appearance and number at all MSG dose levels at both light and ultra-structural levels. However, poorly fixed material was found to resemble the previously reported brain lesion in a newborn monkey.

1404 INTRACELLULAR RESPONSES OF AUDITORY CORTICAL NEURONES TO SIMPLE ACOUSTIC STIMULI. F. de Ribaupierre, M.H. Goldstein, Jr, and G. Yeni-Komshian. Johns Hopkins University, Sch. of Med. Baltimore, USA.

Function and coding properties of the auditory cortex would be better understood if the synaptic inputs to single cells were known. Intracellular records have been obtained for 139 neurons in the primary auditory cortex of unanesthetized, muscle-relaxed cats. Systematic presentation of clicks, noise bursts and tone bursts showed that evoked spike responses are obtained for a considerably smaller set of stimuli than evoked postsynaptic potentials (PSP's). For cells with moderate to high spontaneous activity a close relation was evident between the evoked spike pattern and the PSP's. Many cells had low spontaneous activity, and for them the intracellular technique made apparent inhibitory or subthreshold excitatory synaptic inputs, not reflected in the spike data. The majority of the spike response patterns were transient in nature, but the modification of the cell excitability lasted as long or longer than the stimulus presentation. Active inhibition was usually a component of the evoked synaptic input, and has an important role in determining the pattern of evoked spikes. (Research supported in part by the National Institute of Neurological Diseases and Stroke.)

EFFECTS OF THEOPHYLLINE AND 3'5' AMP ON THE RESPONSE OF THE INTESTINAL VASCULATURE TO NOREPINEPHRINE.* D.R. Richardson. Dept. of Physiology and Biophysics, Univ. of Kentucky, Lexington, Kentucky.

1405

Although cyclic AMP (3'5' AMP) has been widely studied as a mediator of the inotropic effect of cardiac tissue, little attention has been directed towards possible effects of this nucleotide at other levels of the cardiovascular system.

The purpose of these experiments was to directly examine the possible participation of 3'5' AMP in the alpha adrenergic activity of the peripheral vascular. This was accomplished by studying the degree to which 3'5' AMP and theophylline, a blocker of the enzymatic breakdown of the cyclic bond, modulate the constrictor effect of norepinephrine infused into the arterial supply of an isolated section of the small intestine of domestic cats.

It was found that 3'5' AMP or theophylline alone were vasodilatory to the intestine as evidenced by a dose dependent decrease in intestinal vascular resistance (pressure/flow). However, when infused with norepinephrine, both substances potentiated the alpha constrictor effects of this catecholamine. These results suggest that alpha adrenergic responses of the peripheral vasculature are mediated by 3'5' AMP.

*Portion of these studies performed in the Department of Physiology, University of Arizona, Tuscon, Arizona during tenure of a Predoctoral fellowship (NIH 1-F1-GM-28,G51).

A FUNCTIONAL RELATIONSHIP BETWEEN ANGIOTENSIN AND VASOMOTOR TONUS

M. RIEU, D. WASSERMANN, J. MALMEJAC. Laboratory of Physiology Faculty of Medicine COCHIN - PORT-ROYAL. (Associated team of C.N.R.S. Director J. MALMEJAC).

We have shown that the hypertension due to the endovenous contribution of Angiotensin is regulated by the action of baro-depressive zones. Their intervention is, in fact, complex.

intervention is, in fact, complex.

The baro-depressive reflex causing a decrease in the vascular tonus directly intervenes to limit hypertension. However, experimental analysis shows that this is not the only mechanism at work.

The vasomotor tonus is, in effect, one of the supporting elements of the vasoconstrictor action of Angiotensin.

One demonstrates this by the irrigated kidney technique "in situ".

Although the kidney remains under central nervous control, an injection of Angiotensin by the venous pathway provokes a vasoconstriction. This action is clearly diminished after denervation of the kidney and reappears during perfusion with Noradrenaline.

CHANGES IN THE MAINTAINED DISCHARGE OF SINGLE VISUAL CORTICAL CELLS AFTER PROLONGED ADAPTATION AT DIFFERENT LIGHT BACKGROUNDS. E.Riva Sanseverino and L.F.Agnati. Inst. of Physiology, Univ. of Bologna, Bologna, Italy.

In the present investigation the effects evoked by prolonged adaptation at different light backgrounds have been studied on the maintained discharge of single neurons in the striate area 17 and non-striate areas 18 and 19 of the cat cerebral cortex. The animals were unanaesthetized, Flaxedil-paralyzed and artificially ventilated under continuous control of the $\rm CO_2$ expired. Two or more of four fairly different light backgrounds, corresponding to $\rm 2\cdot 10^{-3}$, $\rm 4\cdot 10^{-2}$, $\rm 9\cdot 10^{-2}$ and $\rm 2\cdot 10^{-1}$ cd/m², were presented in random sequences to the cat eyes. The adaptation time for each luminous level was 30-90 min; the greater the difference in light background between two consecutive levels, the longer was the adaptation time. The analysis of the data obtained from 71 neurons showed that the mean frequency of discharge was directly related to changes in the level of the light background for striate neurons, whereas it was inversely related for non-striate neurons.

1406

1408 ARTERIAL ELASTIN FUNCTION*. Margot R. Roach. Depts. of Biophysics and Medicine, Univ. of Western Ontario, London 72, Canada.

Elastin forms an integral part of arteries, but its exact physiological role is unknown. We have attempted to assess the normal function of elastin by studying how pathological processes alter the elastic properties of arteries in the elastin part of the tension-length curve. Arteries exposed to low frequency vibration from heart murmurs or a sound generator (50-300 Hz) became more distensible. Arteries from older patients were stiffer, probably due to changes in both elastin and collagen. Intracranial aneurysms, which are known to contain fragmented elastin, were also very indistensible, and this lead to an increased risk of rupture. We produced similar elastic changes in isolated human cerebral arteries which have a single elastic membrane by exposing them to pressures of 180-200 mm Hg three times. This appeared to fragment the elastin. Since alterations in elastin produce radical changes in the elastic properties of arteries, normal elastin must play a key role in allowing arteries to tolerate physiological pressure changes.

*Supported by Ont. Heart Fndn. and Med. Res. Council of Canada.

SOME CHARACTERISTICS OF PACEMAKER ACTIVITY IN APLYSIA NEURONS. F.A. Roberge and P.A. Mathieu. Center for Neurological Sciences, University of Montreal, Montreal, Canada.

Pacemaker neurons in the abdominal ganglion of Aplysia have a pacemaker locus and a spike trigger zone located on the soma. The characteristics of pacemaker activity in bursting neurons were studied by blocking the spike generating mechanism with tetrodotoxin (TTX). Using intracellular recording, repeated observations of transmembrane potential changes were made during and following the gradual disappearance of spike activity in neurons L6 and R15. Membrane potential oscillations were seen in the steady state following TTX treatment, with periods of 10-40 sec and amplitudes ranging from 5-25 mV. Both the amplitude and period of the oscillation decreased with membrane depolarization and increased with hyperpolarization. The relations are fairly linear for a small range of membrane depolarization and become nonlinear with hyperpolarization. These oscillations are clearly at the origin of bursting activity in neurons L6 and R15. Their sensitivity to changes in membrane polarization indicates that the bursting frequency can be modulated by synaptic input. Although the underlying mechanism of these oscillations is not completely understood, there is evidence that it is closely related to active sodium transport across the membrane.

1410 METABOLIC PARAMETERS IN MYOCARDIAL ISCHAEMIA. M.A.Robertson and J.Grayson., Dept. of Physiology, University of Toronto, Toronto, Canada.

Coronary sinus blood and composition are frequently assumed to normally represent left ventricular metabolism. In animals and man with coronary artery lesions there is spatial and temporal non-uniformity of myocardial perfusion. Coronary sinus blood is now a weighted integral of left ventricular events with under-perfused areas contributing less to mixed venous effluent. Using anaesthetized dogs oxygen consumption and tissue heat production were monitored across an experimentally induced (occlusion of left anterior descendens) ischaemic region of myocardium. Venous effluent was sampled from a small surface vein draining the region so as not to totally impede coronary venous return. Local tissue flow and heat production (L.H.P.) were recorded using heated thermocouple probes implanted in the myocardium. The flow measurements in thermal conductivity units were multiplied by A-V oxygen differences to give the oxygen consumption index (O.C.I.). The O.C.I. and L.H.P. were compared at half-hour intervals pre- and post-occlusion. Flow and L.H.P. were also recorded in an adjacent non-ischaemic region of left myocardium. Pre-liminary experiments have shown good correlation between the O.C.I. and L.H.P. Both parameters declined significantly post-occlusion. Transient increases to near pre-occlusion levels occurred over a six hour post-occlusion period. No significant changes were observed in the non-ischaemic region.

INFLUENCE OF NEPHRON HETEROGENEITY ON RENAL UREA EXCRETION. F. Roch-Ramel, P.C. Gardaz and G. Peters. (Inst. pharmacol., Univ.of Lausanne, Switzerland)

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In rats overloaded with urea TF/PU/TF/PIn found in superficial end-distal tubules was lower than U/PU/U/PIn (Pelvic urine) (1). Apparent addition of urea to collecting duct fluid also occured under angiotensin-amide (.2 ug/kg min) and, under particular conditions, in animals infused with 5% NaCl (.01 ml/rat/min). The ratio of superficial to juxtamedullary single nephron GFR (2) was .63 $^\pm$.04 (4 rats, 199 nephrons) in controls (non-diuretic and mannitol infusion), vs. .39 $^\pm$.05 urea overloading (4 rats, 440 nephrons) and .49 $^\pm$.03 angiotensin-amide (3 rats, 164 nephrons). The contribution of deep nephron filtrate to total pelvic urine was thus increased. This increase may contribute to apparent addition of urea to fluid flowing through collecting ducts.

(1) Roch-Ramel F. et al., Am. J. Physiol. 218, 1524, 1970. (2) Baines A.D. and de Rouffignac C. Pflügers Arch. 308, 260, 1969.

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BIOCHEMISTRY OF AGING AND ITS ENDOCRINE CONTROL. M. Rockstein. Dept. of Physiology, Univ. of Miami, Schl. of Medicine, Miami, Florida, U.S.A.

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In the newly-emerged male house fly there is a programmed rise in flight ability, as well as size of the giant mitochondria in the flight muscle, both of which reach a peak level by the fourth day. Conversely, failure in flight ability, marked by the onset of wing abrasion sometime within the fourth to fifth day of adult life, culminates in complete wing loss, beginning with the sixth day, with more than 95% of the population being completely wingless by the onset of the third week. Mitochondrial Mg-activated ATPase activity likewise reaches its peak on the fifth to sixth day whereas extramitochondrial NAD-dependent &-glycerophosphate dehydrogenase reaches its peak level at the fourth day of male adult life. Corresponding age-related substrate content, including ATP, ADP and AMP, trehalose and thiamine, confirm the presence of a complex interdependent pattern of biochemical changes underlying the aging of motor ability of the male fly. Surgical removal of wings immediately following complete extrusion produced no change in the normal age-dependent pattern of Mg-activated ATPase activity in the male thoraces, whereas the ≪-glycerophosphate dehydrogenases activity attained and remained at its fourday peak throughout life, even following such surgical removal of wings. Current studies indicate a dependency of initial development of flight ability upon the distribution of the neurosecretory material of brain cells, particularly in relation to the mobilization of trehalose from glycogen, and development of flying ability.

1413

ZUR WIRKUNG DER QUECKSILBERDIURETIKA AUF DEN Na+ UND K+ -MEMBRANTRANSPORT DER MENSCHLICHEN ERYTHROZYTEN UND RATTENLEBERMITOCHONDRIEN. M.Rocsin, M.Rocsin. Lab.f.Pharmakodynamie, Med.Inst., Timişoara, Rumanien. Im Rahmen unserer Untersuchungen über die extrarenale wirkung der Quecksilber-Diuretika (QD) haben wir unsere Aufmerksamkeit auf die menschlichen Erythrozyten und auf die Mitochondrien der Rattenleber gelenkt. Wir untersuchten die Permeabilität der Membranen bzw. den aktiven und passiven Kalium- und Natriumtransport durch QD in einer Konzentration von 2 bis 20 mM/L Wir verwendeten sowohl bekannte Diuretika (Salyrgan-Höchst, Novurit-Chinoin), als auch einige von uns präparierte Quecksilberverbindungen des Cyclohexandicarboxylsäureamids. Die Untersuchungen an den Rattenlebermitochondrien ergaben nach der Verabreichung des QD einen Anstieg der Mitochondrien-Quellung von 9-12 Einheiten im akuten Experiment und von 10-28 Einheiten im chronischen Experiment. Die Aktivität der Succindehydrogenase fiel hingegen von 74 auf 68 Einheiten im akuten und von 60 auf 56 Einheiten im chronischen Experiment. Zugleich konnte im akuten Experiment unter der Wirkung der QD ein Anstieg des Natriumgehaltes von 120 auf 200 m.val./mg Eiweiß und ein Abfall des K von 136 auf 94 m.val./mg Eiweiß in den Mitochondrien nachgewiesen werden. Aus unseren Versuchen ergibt sich somit eine parallel verlaufende Elektrolytverschiebung, sowohl in den Erythrozyten als auch in den Lebermitochondrien.

1414 MYOCARDIAL COMPARTMENTS, LYMPHATICS AND CONNECTIVE TISSUES. Simon Rodbard.
Department of Cardiology, City of Hope Medical Center, Duarte, California 91010.

Analysis of tissue architecture (Med. exp. 19:65, 1969) shows the mammalian ventricle to consist of seven discrete compartments, each with its specific structural characteristics and lymphatic system. Liquid methyl methacrylate mixed with a selected pigment was injected intramuscularly into discrete sites of the myocardium in more than 300 hearts. After the plastic hardened, digestion of the tissues released the cast which had been formed. Casts of the free right ventricular wall of mammals consist of parallel hoops, interdigitated with, but separated from the septum. The left ventricular free wall consists of spiral staircases of steps wound around newels which extend from epicardium to endocardium. Epicardium at the interventricular sulcus consists of septum. Two outflow (conus) and two inflow compartments are demonstrated in the base of the heart. Casts of the right and left bundle have also been obtained. In related studies, myocardial ghosts have been produced by immersing hearts in 0.1% KOH for one month. Approximately 2% of the original wet weight remained as collagen and elastin. These approaches provide new bases for the study of depolarization patterns, pumping action, volume/pressure relationships, and other functional characteristics of the heart. (Aided by HE 08721, NIH.)

1415 MONOAMINERGIC CONTROL OF INSULIN SECRETION. R.R.Rodríguez, R.E.Hernández and J.J.Gagliardino. Inst. of Physiology, Sch. of Med., Univ. of La Plata, Argentina.

The role of intracellular pancreatic monoamines on insulin secretion was studied in the rat applying several experimental approaches. Two different monoamineoxidase inhibitors (nialamide and tranylcypromine) elicited a sig nificant insulin release both in vivo and in vitro. On the other hand, the study of pancreatic monoamines content using fluorescence and chemical tech niques, serum glucose and immunoreactive insulin (IRI) levels following the administration of the natural monoamines precursors showed different results. The injection of L-dihydroxyphenylalanine (DOPA) was accompanied by an increase in the dopamine content within the pancreatic β cells without any changes either in the serum glucose or the IRI levels. The aminoacid was also unable to stimulate the in vitro insulin secretion. Conversely, Ltryptophan administration was followed by a marked increment in the pancrea tic and blood serotonin content as well as a rise in the serum IRI levels and a significant drop in the serum glucose levels. Moreover, serotonin induced a significant in vitro insulin release. None of these changes were ob served when tryptophan metabolism was hampered using an aromatic decarboxylase inhibitor. All these results pointed out the outstanding role of monoa mines in the control of rat insulin secretion.

NEW DATA ON NEGATIVE COMPONENTS OF THE DIRECT CORTICAL RESPONSE.

A.I.Roitbak. Inst. of Physiology, Georgian Academy of Sciences, Tbilisi,
USSk.

Under deep anesthesia the dendritic potential (DP, 20-30 msec) reflects "monosynaptic" EPSPs of the apical dendrites. The DP is increased under the influence of eserine, Ca⁺⁺ and decreased by Mg⁺⁺, Br and caffeine; the GABA application results in its abolishment, strychnine, morphine and adrenaline being ineffective. The post-tetanic depression lasts more than 20 min. and is observed more frequently than the post-tetanic potentiation. The slow negative potential (SN, 300-3000 msec) is recorded in the superficial cortical layers. There are data indicating the participation of the neuroglia in the SN genesis. The SN is associated with the depression of the DP and of discharges of the cortical neurons. It is augmented by Ca⁺⁺, GABA, anode of DC current and decreased or abolished by Mg⁺⁺, Br , cathode of DC current, strychnine, morphine, caffeine and X-rays.

REGULATION OF AMP DEAMINASE FROM VERTEBRATE SKELETAL MUSCLES. G. Ronca, A. Raggi, M. Ranieri and S. Ronca-Testoni. Inst. of Biochemistry, Univ. of Pisa. Pisa, Italy.

1417

The skeletal muscles have higher content of AMP deaminase than all the other tissues, including heart and smooth muscles; in skeletal muscle the catabolism of AMP essentially depends from this enzyme. Rat AMP deaminase has the molecular complexity and the kinetic behaviour of regulated enzymes. At physiological concentration of AMP it is activated by monovalent cations with the following order of effectiveness K⁺> Na⁺> Li⁺> NH₄⁺. Nucleoside triphosphates (NTP) inhibit the enzyme activated by KCl; inorganic phosphate (Pi) and creatine phosphate (CP) are also inhibitors. The inhibition by these compounds is removed by ADP. The enzyme from frog, pigeon, rabbit and guinea pig muscles behaves similarly to the rat enzyme. The data suggest that when ADP accumulates in muscle, the inhibition by NTP, Pi and CP is removed and the AMP is deaminated to IMP(IMP, on the contrary of AMP, is neither substrate nor inhibitor of myokinase). In this way the enzyme contributes with myokinase to maintain a high ATP/ADP ratio, even when the breakdown of ATP overcomes its synthesis. The removal of AMP appears to be more important in fast muscles since AMP deaminase activity is higher in fast than in slow muscles.

Supported by a grant of the Italian Consiglio Nazionale delle Ricerche.

ORGANIZATION OF THE PROJECTION FROM MOTOR CORTEX TO DISTAL FORELIMB MUSCLES IN THE MONKEY. I. Rosén and H. Asanuma. Dept. of Physiology, New York Medical College, New York, New York USA.

1418

Efferent neuron colonies projecting to individual hand muscles were explored by intracortical microstimulation. Cebus monkeys were used. Under Halothane anesthesia a closed chamber was attached to the skull over the exposed precentral gyrus and bipolar EMG electrodes were implanted into forelimb muscles. Wounds were infiltrated with a long-lasting local anesthetic (Zyljectin). The experiments were carried out with tranquilizing doses of Nembutal (4-5 mg/kg). Trains of pulses of 30 msec duration (0.2 msec pulse width, 300 cy/sec) were delivered through the microelectrode into the depth of the cortex and the effects were monitored either by EMG or by observing finger movements. The penetrations through the cortex were later reconstructed on histological sections. It was found that the thresholds for eliciting forelimb muscle contractions were lower in monkeys than in cats. Cortical efferent zones which produce different movements of a finger (extension, flexion, abduction, adduction) were located in distinctly separate but adjacent parts of the cortex. The individual efferent zones extended from the surface to the depth of the cortex along the direction of the radial fibers. The experiments demonstrate a discrete spatial organization within the cortex with cortical columns controlling individual hand muscles. (Supported by USPHS, NIH Grant NS-09095).

1419

DYNAMICS OF ARTERIAL BLOOD PRESSURE RESPONSES TO SINUSOIDAL WORK LOAD IN MAN. G. Rosenhamer and O. Wigertz. Dept. of Physiology and Medical Physics, Karolinska Institutet, Stockholm, Sweden.

Systolic, diastolic, mean and pulse pressures in the radial artery, and heart rate in 7 physically active young men were subjected to frequency analysis by using sinusoidal work load as a forcing function. Subjects exercised in the supine position on a cycle ergometer. With the pedalling rate constant, the work load was varied sinusoidally over a range of drive frequencies between the two fixed extremes of 250 and 1050 kpm/min. Predicted step responses obtained by applying the transfer functions estimated for radial systolic and pulse pressures showed close similarity to observed step responses, indicating linear properties of the underlying systems. Using known characteristics of the peripheral distortion of the pressure pulse, the responses of both the radial and central systolic and pulse pressures to work load could be described by second-order transfer functions. Resonance occurred for periods near 7 min, indicating overshoots for both variables in the time domain. The absence of a resonance feature for the heart rate suggests baroceptive inhibition of this variable. The changes in radial diastolic pressure were small and not clearly related to the drive frequency. The response of the radial mean pressure could not be described accurately by either first- or second-order functions, but exhibited phase lead features, suggesting sensitivity to rate of change in work load.

1420 DIFFERENT TYPES OF THE VENTRICLE MYCCARD ACTIVATION OF VERTEBRATES. M.P.Roshchevsky. Inst. of Biology, Academy of Sciences of the USSR

Komi Branch, Syctyvkar, USSR.

Vertebrates produced several types of myocardial activation during evolution, due to environment and load of the heart. In fishes myocardial activation runs along the main axis of the ventricle (v.)in subepicardial and subendocardial layers simultaneously. The v.activation in amphibia begins in the a.-v.fissure.Excitation of caudata amphibia is shifted to apical area and then to the base along all depths of the ventricular wall simultaneously. The base of ecaudata amphibia v. is activated before the apex and excitation is passed from internal to external layers. V. activation in reptiles is due to appearance of weakly differentiated conducting fibres but probably the activation is spread mainly along myocardial paths. In birds Furkinje fibres are perfectly developed, run through the whole myocardial wall and provide consecutive excitation of different v.areas beginning from right apex. Left v. wall is excited almost simultaneously through all its depth. There are at least two types of myocardial activation in mammals. One is the well studied type of v.activity in man and carnivores. The other is revealed in artoodactyla and perissodactyla characterized by "explosion, flash" of excitation occurring simultaneously in extensive zone of walls in left and right ventricles.

RESEARCHES ON RELATIONS ESTABLISHED DURING PHYSICAL FATIGUE, BETWEEN SERUM 1421 AND CSF PROTEIN COMPONENTS. C.Rotaru, V.Rosca. Dept. of Physiology, Faculty of Medicine, Iassy, Romania.

Studies were performed on dogs subjected to exercises (running on the tread-mill); proteins, total mucoproteins and active mucoproteins in the Donaggio reaction were assayed in blood and CSF sampled during rest and after cessation of the graded exercise. Mathematical-statistical analysis of the results gave significantly elevated values of all the protein components during fatigue as compared to rest, both in the blood and the CSF. The blood mucoprotein/total protein % ratio showed a definite and permanent elevation of mucoprotein specific weight during fatigue versus rest, but behaved differently in the CSF with no consistency in the curve of absolute values and in the differences found during fatigue as compared with rest. These features prove the involvement of a regulating function in the distribution of protein components in the two fluid compartments of the body during physical effort and fatigue.

1422 GENERAL ANESTHETICS EXPAND MEMBRANES AT SURGICAL CONCENTRATIONS. S. Roth and P. Seeman. Pharmacology Department, University of Toronto, Toronto 5, CANADA.

Surgical concentrations of halothane, chloroform, ether and methoxyflurane protect human erythrocytes from osmotic hemolysis. The MAC (MINIMUM ALVEOLAR CONCENTRATION) values required for human anesthesia are identical to the concentrations which produce 8% anti-hemolysis (AH₈₇) of human erythrocytes. These AH₈₇ values are 2 x 10⁻⁴ M for halothane, 7.7 x 10⁻⁴ M for chloroform, 8.2 x 10⁻³M for ether, 2.8 x 10⁻⁴ M for methoxy-flurane and 2.2 x 10⁻¹ M for ethanol, and were obtained at 24 °C; the AH₈₇ values are 25% higher at 37 °C which makes them then identical to the values for MAC.

This 8% reduction in hemolysis occurs because of an expansion of the erythrocyte membrane by 0.4% in surface area (Biochim. Biophys. Acta 183, 490, 1969). This anesthetic--induced expansion of 0.4% is of the same order as the estimated 0.1% expansion of the luminescent protein system when exposed to general anesthetics (Eyring, Science 154, 1609, 1966). If the same physico-chemical processes occur in excitable membranes, then it can be concluded that general anesthesia is associated with a membrane expansion of 0.4%; for local anesthesia the amount of membrane expansion is about 2-3%.

It is conceivable that the simple anti-hemolysis test to determine the AH_{87} may be useful in predicting the MAC for an individual person. (Supported by grant MA-2951 of the Medical Research Council of Canada, the Ontario Mental Health Foundation, and the

Ontario Alcoholism and Addiction Research Foundation.)

STUDIES ON NATURAL VARIATION IN MITOTIC INDEX OF THE FROG LENS EPITHELIUM. H. Rothstein and D. Rosenbaum. Dept. of Zoology, University of Vermont, Burlington, Vt., U.S.A.

1423

Diurnal and seasonal variations have been reported to occur in the lens epithelium of mammalian and amphibian organisms. For some years our laboratory has been studying injury and explantation-induced proliferation in the lenses of anurans. The possibility exists that natural rhythms in mitotic activity could heavily influence the results of experiments such as those just indicated. We have therefore undertaken a study of possible fluctuations in mitotic activity due to age, time of day, and month of the year (in both R. catesbeiana and R. pipiens). The major conclusion of this work is that the variations in mitotic index in a given group of animals is greater than the differences in the averages between groups sampled at various times. Furthermore, the mitotic index of the lens prior to injury or explantation cannot serve as a reliable criterion by which to estimate the amount of mitosis these treatments elicit. Our age studies are not yet complete for we have examined animals no younger than 11 months (post-larval) of age. It is expected that in younger frogs (as in other vertebrates) the M.I. will be significantly higher than in the older organisms.

This work was supported by USPHS Grant EY 00281-07.

JUNCTIONAL MEMBRANE PERMEABILITY; DEPRESSION AND RESTORATION. Birgit Rose Cell Physics Lab., Dept. Physiol., Col. P & S, Columbia Univ., New York, N.Y., USA

1424

Cells of the salivary gland of Chironomus thummi are in direct ionic communication with each other: electrophoretically injected small ions, fluorescein, and procion yellow pass freely from one cell interior to the next through membrane regions of high permeability ("junctional membranes"). Junctional membrane permeability is depressed irreversibly by long-term substitution of Li for extracellular Na, reversibly by long-term lack of extracellular Ca and Mg, and by treatment with 10-5-5x10-4 M DNP. The depression is accompanied by cell depolarization in all cases. Junctional membrane permeability is restored by repolarization of the cells with inward current. The results are explainable, in terms of Loewenstein's hypothesis (J. Coll. Interface Sci. 25, 34, 1967), by known mechanisms regulating cellular Ca²⁺; the depression of junctional permeability, by a rise of the normally low level of cytoplasmic free Ca, and the restoration, by a return to the normal level.

1425

SUSTAINED EVOKED POTENTIALS, SPREADING DEPRESSION AND METABOLIC ACTIVITY OF THE CEREBRAL CORTEX MEASURED IN SITU. M. Rosenthal and G. Somjen, Dept. of Physiol. and Pharmacol., Duke Univ., Durham, N. C., U.S.A.

Microcapillary electrodes with DC-coupled amplifiers were used to record sustained shifts of the potential of the intact cerebral cortex of cats. Sustained potential shifts were evoked by stimulating either the surface or thalamic nuclei (VB) by repeated electrical pulses. Spreading depression was provoked either by electric stimulation of the surface or by superfusion with Ringer solution containing abnormally high K* concentration Metabolic activity at the surface of the cortex was measured by the intensity of fluorescence emitted at 460 mµ when the tissue was illuminated by light of 366 mµ. The intensity of the fluorescence signal is related to the oxidation-reduction level of intramitochondrial NADH. The amplitude of sustained evoked potentials and the oxidation of NADH showed a linear positive correlation. Spreading depression was also associated with a decrease of the intensity of fluorescence, at times by as much as 30% of the total. There was no statistical correlation, however, between the amplitudes of fluorescence decline and the potential shift in SD. These findings are compatible with the suggestion that a substantial part of oxidative metabolism is spent in the active transport of ions released from neurons during excitation and during spreading depression. (Supported by N.I.H. grants NS06729 and NS05330)

1426 MECHANISM OF ACTION OF OESTROGENS ON MUSCULAR EXCITABILITY. I. Rosner and B. Rosner. Inst. of Norm. & Path. Physiol. - Prof. D. Danielopolu - Bucharest, RUMANIA. Present address: Centre de Recherche Winthrop, 21 - DIJON D, France.

Chronic experiments (1220 determinations) were carried out on 15 rabbits; strength duration curves and chronaxy of the flexor of the hindpaw were determined daily. Single injections of oestrodiol (0.125 - 0.625 mg/kg body weight) decrease chronaxy in females for 1 - 4 days. This effect is not present in males and in hysterectomised females. Repeated administration of oestrodiol (0.125 mg/kg b.w./day) for periods of up to 20 days determines the shortening of chronaxy during the treatment period in normal females. After an interval of 1 - 5 days, the cessation of treatment leads to a disappearance of the effect. The same treatment fails during the first 15 days to determine muscular excitability changes in hysterectomised females and in males; after this period, a decrease in chronaxy appears and persists for many months in spite of the suppression of treatment. Therefore oestrogens act on muscular excitability by two mechanisms: one rapid and of short duration, necessitating the presence of the uterus and probably of reflex nature, and the other, slow and persistent, appearing only in the absence of the uterus.

1427 REACTION OF SPINAL MOTONEURONES TO MUSICAL SOUNDS. S. Rossignol. Aviation Medical Research Unit, McGill University, Montreal, Canada.

Preceeding experiments have shown that in man there is a preferred frequency of hopping on one leg of 2.0 to 2.2 jumps/sec. Furthermore, it is intriguing to find that much dance music is rhythmically structured around this frequency. This striking similarity led to an investigation of the hopping cycles in 5 subjects jumping on a piece of traditional fance music in synchrony with the down beats occurring regularly at 490 msec intervals. these experiments, it was found that all subjects maintained a periodicity of jumping of 490 msec with a standard deviation of ± 16 msec and that all landings in all subjects anticipated the beat by 50 msec with a standard deviation of ± 11 msec. This precision in the regularity of jumping attained with music suggested there might be a direct cochleo-spinal effect of musical auditory stimuli influencing the timing of reflex motor events related to jumping. To verify this hypothesis, the level of excitability of the spinal motoneurone pools was tested by the H-reflex technique at every 20 msec after the administration through earphones of a 1 Kc sinewave tone burst of 50 msec duration repeated at every 30 seconds. Preliminary results show at least a twofold increase of this excitability after a latency of 70 msec and lasting approximately 100 to 200 msec. These results suggest that sounds might indeed influence, at the spinal level, the timing of motor events when hopping to music at the preferred frequency.

1428 EFFECT OF SYMPATHETIC STIMULI ON RAT MAST CELLS. A.M.Rothschild and Mercedes P.Oliveira Antonio. Dept.Pharmacology, Faculty of Medicine of Ribeirão Prêto, University of São Paulo, Ribeirão Prêto, Brazil.

The effects of catecholamines and of sympathetic activity on rat mesentery mast cells have been correlated with histamine release. These effects involve stimulation of alfa-type receptors on the mast cell since they are inhibited by alfa, but not by beta-sympatholytics and produced by adrenaline and nor-adrenaline, but not by isoprenaline. In-vivo, significant alterations of mesentery mast cells were observed in rats submitted to exercise (10 min swimming), cold exposure (10 min, 8°C), destruction of carotid sinus pressor receptors, stimulation of the splanchnic nerve and the injection of tyramine. The sympathetic system seems to have a functional relationship with the mast-cell leading to discrete histamine release. A physiological function for histamine, apart from its secretagogue action has long been sought for: we suggest a modulatory role for mast-cell histamine, acting to correct excessive local effects of catecholamines. Aided by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

GLOMERULAR FILTRATION RATE OF SINGLE SUPERFICIAL AND JUXTAMEDULLARY NEPHRONS DURING HYPOTENSION BY AORTIC CONSTRICTION. C. de Rouffignac, P. Benceáth, J-P.Bonvalet, with the technical assistance of S.Deiss. Dept. of Biol., CEN - SACLAY, 91, France.

1429

The immediate effect of a reduction in arterial blood pressure (BP) on single glomerular filtration rate (sgfr) has not yet been studied. Therefore, sgfr of superficial (S) and juxtamedullary (JM) nephrons of 12 nondiuretic (ND) rats has been measured in the minute following controlled aortic constriction (82>BP>38 mmHg), using the 14-C ferrocyanide infusion technique. As compared to data from 10 control animals (130>BP>93 mmHg; sgfrS=32.7-1.4 S.E.M., sgfrJM=41.1-1.9-11/min), sgfr's were unchanged in 5 rats with BP ranging from 82 to 68 mmHg (sgfrS=30.2-0.7, sgfrJM=41.1-2.6 nl/min) but decreased sharply in the other ones with BP between 63 and 38 mmHg.At 38 mmHg, sgfr's were:S=2.2-0.6 and JM=4.2-3.0 nl/min. These observations allow to infer that in ND rats sgfr must cease at 35 mmHg and that the effective filtration pressure equals to about 30 mmHg.Micropuncture data, reported by others and obtained necessarily during prolonged hypotension, indicate that sgfr's are already diminished in the 85-65 mmHg BP range. Employing the present technique, a similar decrease in sgfr's was found in 5 other ND rats, subjected to prolonged (90 min) hypotension (78>BP>65 mmHg; sgfrS=21.6-2.4, sgfrJM=26.6-2.7 nl/min). These results suggest that during arterial hypotension by aortic constriction sgfr depends not only on the BP level and that other timedependent factors ought to be considered. No intrarenal redistribution of sgfr could be observed in any of the animals of the present studies.

CHANGES IN THE MOTOR ACTIVITY OF THE RUMEN AND IN THE GLYCAEMICAL LEVEL IN SHEEP AFTER ADMINISTRATION OF DIHYDROERGOTAMINE AND ERGOTAMINE. V.Roussev, E.Bocheva, A.Petkov. Physiology Dept., "G.Dimitrov" Higher Agricultural Institute, Sofia, Bulgaria.

1430

Experiments have been conducted with 6 sheep with fistulae of saccus ruminis dorsalis. After Dihydroergotamine (2 mg/30 kg liveweight i.m.) or Ergotamine (0.01 mg/kg liveweight i.m.) has been introduced, the movements of the rumen become weaker or cease for 2 or 3 hours, while the level of blood sugar increases. However, the changes in the glycaemical level and in the movements of the rumen are not always synchronous. The restoration of the rumen motor activity precedes the normalization of the glycaemical level. There are cases, when the movements of the rumen weaken and the glycaemical level practically does not change or increases very slightly. This demonstrates that no direct relationship exists between the movements of the rumen and the level of blood sugar. The investigations give grounds to assume that the sympathicoadrenal system is of significance for the motor activity of the rumen.

ROLE OF BLOOD PRESSURE CHANGES IN HUMAN SPLANCHNIC VASCULAR RESPONSES TO HYPERTHERMIA.

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1431

Our question was whether falling arterial blood pressure (BP) during hyperthermia in resting man is a major stimulus for increasing splanchnic vascular resistance (SVR). In 7 men, skin temperature (T_S) was controlled via water perfused suits at 34-36°C (control, period I) and at 40-41°C (heating, period II). During periods I and II we measured splanchnic blood flow (SBF), BP, and in 4 men cardiac output (CO). During the first 35 min of period II CO increased 2-times. BP fell 10%. TPR fell 52%, SBF fell 36% and SVR rose 38%. At 35 min into period II, circulation to both legs was totally occluded for 10 min. During occlusion BP rapidly rose to (or above) control, while CO rose an additional 5%, TPR rose 13%, SBF rose 11% and SVR did not change, all with respect to pre-occlusion values. After release of occlusion sudden cooling of T_S produced a fall in BP but CO and SBF gradually returned toward control. We conclude that during hyperthermia stimuli other than falling of changing BP command SVR. So far one experiment using lower body negative pressures to reduce BP and displace blood peripherally indicates that SVR does respond to baroreceptor stimulation in normothermia.

1432 COMPARISON OF THE ELECTROPHYSIOLOGICAL PROPERTIES IN THE HEART MUSCLE CELLS OF VARIOUS INSECTA SPECIES. K.S.-Rôzsa and I.V.-Szöke. Biol.Res.Inst.of the Hungarian Academy of Sciences, Tihany, Hungary.

Electrophysiological properties of the heart were studied in Locusta ... migratoria, Mantis religiosa, Ephippigera ephippiger, Tettigonia viridissima and Gryllotalpa vulgaris by microelectrodes. The resting potential never exceeded 40 mV and the maximal value of the action potentials was 50 mV. The action potential showed always overshoot. The duration of the action potentials was between 30-170 msec. According to their form, the action potentials were in most of the cases of pacemaker type, and plato type potentials were registered only in the hearts of Mantis Ephippigera. Contrary to the literature, the generation of the action potentials — similar to mammalian and molluscan hearts — was in all investigated Insecta Nat-dependent and the spike generation does not depend on the Mg**ions. The Ca**ions take part in the maintenance of the amplitude and rate of the spike potentials.

1433 INCREASED REM SLEEP IN THE CAT AFTER FOOD INTAKE. E.H. Rubinstein and R.R. Sonnenschein. Dept. of Physiology, UCLA School of Medicine, Los Angeles, Calif. 90024 U.S.A.

The instillation of fat (1 ml corn oil) into the duodenum of awake instrumented cats promoted sedation and sleep (Fara, J.W., Rubinstein, E.H., Sonnenschein, R.R. Science, 1969, 166:110-111). Total sleep time, on 3-hour sessions, was increased from 33 to 48% in association with an increase in the number of REM episodes. In other cats, the intake of a single large meal prior to the 3-hour recording sessions, also increased the duration of total sleep, from 46 to 55% together with an increase in the REM stage, from 8 to 14% and the number of REM episodes. In other animals, recovery from denervation of the gut (bilateral splanchnicectomy and abdominal vagotomy) was followed by a decrease in total sleep time, but after a single large meal, they also displayed an increase in REM sleep and the number of REM episodes. These results support the hypothesis that gastro-intestinal hormones, released by the presence of food into the visceral lumen, may participate in the regulation of the sleep-wakefulness cycles. Supported by grants from USPHS (HE-05157), Amer. Heart Assn. (69880 & 69127) and Los Angeles County Heart Assn. (4371G).

A MODEL FOR STUDIES OF MYOTONIA IN VITRO. R. Rüdel and J. Senges.

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2,4-Dichlorphenoxyacetate (2,4-D) has long been known to produce symptoms in living rats very similar to those of myotonia. Its usefulness for providing a model of myotonia in vitro was questioned by the findings that there is no change in the resting membrane potential, nor any spontaneous firing of muscle fibres from 2,4-D treated isolated rat diaphragm. (Hofmann et al., Electroenceph. clin. Neurophysiol. 21: 521-537; 1966) However from the same preparation, Stein and Kuhn (Klin. Wschr. 43: 328-330; 1968) reported a markedly slowed relaxation after contraction under 2.5 mM 2,4-D, particularly after omission of Ca from the bathing solution. Electromyographic studies of the isolated rat diaphragm 2 min after application of 2,4-D show "dive-bomber" volleys typical of myotonia, suggesting that the accompanying retardation of relaxation is due to some muscle fibres continuing to fire for about 1 s after the directly applied 0,5 ms stimulus. Addition of 10-g/ml curare to the bathing solution does not abolish the continued firing and slowed relaxation and thus proves the myogenic origin of the effect. 2,4-D, therefore, need not be metabolized in the body to generate myotonic effects. - Supported by the Deutsche Forschungsgemeinschaft.

SURFACTANT INHIBITION IN VITRO. R. Rüfer. Max-Planck-Institute for Experimental Medicine, Department of Physiology, Göttingen, German.Fed.Rep.

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Surface active substance is believed to form the alveolar surface film on a liquid hypophase. Therefore, the relationships between the lining layer and its hypophase may have some biological relevance. Using the Langmuir—Wilhelmy-technique we studied the influence of various hypophases on the spreadibility of alveolar lung surfactant prepared from rat lungs or of synthetic dipalmitoyllecithin. Area/surface tension diagrams of these films indicated an increase of minimum surface tension if the surface tension of the original hypophase was lowered by the addition of proteins (albumin, globulin, fibrinogen) or detergent (Tween 20). E.g. using Ringer solution for hypophase (surface tension 73 dynes/cm) the minimum surface tension of lung surfactant containing 3 µg lipid phosphorus was estimated to be 15 dynes/cm. The addition of globulin (10⁻² g/100 ml hypophase) caused an increase of minimum surface tension to nearly 30 dynes/cm. This inactivation of surfactant is explained by an inhibition of its spreadibility. The formation of a surface film only occurs if the molecular forces (the surface tension) of the liquid hypophase which tend the surfactant molecules to spreading are greater than the molecular forces which attract the substance itself. Thus it can be suggested that a lowered surface tension of the hypophase can cause an increase of the surface forces in the lung.

PRESSURE-FLOW RELATIONSHIP OF THE PULMONARY CIRCULATION IN MAN. François RUFF, Pierre DUROUX, Isabelle CAUBARRERE and Philippe EVEN. Clinique de Pneumo-Phisiologie, Hôpital Laënnec, 42, rue de Sèvres, Paris 7°, FRANCE and Dept of Physiology, Faculté Necker-Enfants-Malades, Paris 15°

Pressure-flow relationship of the pulmonary circulation has been studied in man.Pulmonary blood flow has been increased by temporary complete occlusion of one pulmonary artery and one lobar artery of the other side.Vascular and esophageal pressures, air flow and volume change were recorded as well as cardiac output, blood volume and blood gases.Pressure-flow relationship in normal man is linear:its slope is 1.3+0.4 mm Hg/l/min/m² and the intercept passes through the origin. The shape and the slope are modified by several factors:1) The effects of increased airway resistances were studied in subjects with chronic obstructive lung diseases. The relationship remains linear but a positive intercept appears on the pressure axis.2) An increase blood viscosity raises both slope and intercept.3) Isoproterenol decreases the intercept, when this intercept is increased.4) On the contrary, exercice increases the intercept.5) An increase in left atrial pressure decreases the intercept (when it is increased). This results suggest that:a) the intercept is related to functional factors; b) the slope is related to viscosity but mostly to anatomical factors; c) in normal man the pulmonary circulation is already fully distended at rest, and also fully recruited.

EFFECT OF VERATRINE ON THE Na CONDUCTANCE OF EEL ELECTROPLAQUES. F. Ruiz-Manresa. Lab. of Neurophysiology, P&S of Columbia University, New York, N.Y. 10032, and Inst. de Medicina Experimental, Universidad Central de Venezuela, P.O. Box 50587, Caracas. Current clamp and A.C. impedance determinations in isolated eel electroplaques de-

Current clamp and A.C. impedance determinations in isolated cel electroplaques demonstrate that veratrine has no effect on the resting conductance of the excitable membrane of this preparation (G_1+G_2). Spike electrogenesis however, is affected by the appearance of a long lasting plateau in the terminal portion of the spike, wich courses with a low membrane impedance, and whose magnitude is dependent on the concentration of the drug. The reversal potential of this plateau is that of the peak of the spike (E_{Na}). Despite the changes in the time course of Na inactivation, the excitability of the G_k system remains unaltered and depolarizing K inactivation persists as in the control. This fact favors the idea of individual, separate pathways for both Na and K. The results also seem to indicate that veratrine acts specifically on previously open Na "channels".

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FREQUENCY-POTENTIATION AS THE INTERACTION OF SEVERAL PARAMETERS.

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The well known force-frequency-relation of the heart muscle is explained on the basis of the assumption of a positive inotropic effect of the frequency stimulation and a negative inotropic effect of the individual stimulus-interval. In the mammalian heart (papillary muscle of guinea pig), the latter effect can be eliminated by stimulus intervals of 1 sec after rhythmical activity. In this range of intervals, the potentiation is maximal and independent of further prolongation of the resting period. Under these conditions, frequency-potentation is present up to 600 stimuli/min. This "true" relationship between force and frequency does not hold for frog heart, in which the tension development seems to be more governed by the duration of the individual action potential. Under consideration of all parameters (time interval of stimulus, "true" frequency potentiation and duration of action potential) it is possible to predict peak and time course of potentiated and depressed contractions under the influence of various rhythmical and arrhythmical stimulation patterns.

1439 ELECTROPHYSIOLOGICAL INVESTIGATION OF THE SIMPLE FORMS OF THE TEMPORAL CONNECTION. V.S.Rusinov. Inst.of Higher Nervous Activity and Neurophysiology, USSR Academy of Sciences, Moscow, USSR.

The formation of temporal connection is accompanied by a steady potential shift of the animal's cerebral cortex, appearing in response to the conditional stimulus. Artificial polarization of the cortex, evoking a DC shift also leads to the formation of the temporal connection but in its simple forms, e.g. a summation reflex or a dominant. Simultaneously the following occurs: the dendritic potential configuration and the form of neuronal activity are changed, the number of the synapses with a great quantity of synaptic vesicles of the V-VI layers of the cortex increase. The most durable changes (up to 1 hour and longer) are observed in intermediate neurons and glial elements.

1440 ELERGY SUPPLY OF THE MUSCLE AFTER HYPOFUNCTION. E. Russanov. Inst. of Physiology, Bulgarian Academy of Sciences, Sofia, Bulgaria.

Studies were made on the skeletal muscles and myocardium in rabbits placed under the conditions of a continuous motor hypofunction. Substantial decrease of glycogen, slighter of creatine phosphate and insignificant decrease of ATP were found. The ratio ATF/ADP was decreased while the potential of redox-system lactate-pyruvate was not changed. These findings are to be accounted for by the contracting proteins and the energy-supplying systems. The contractile function of the muscle cells is closely related to the level of glycogen. Conclusion emerges that the energy supply of the muscle after hypofunction is adapted to the level of the physiological functions.

A PERIPHERAL APHAGIC SYNDROME. M. Russek & R. Racotta. Dept. of Physiol. E.N.C.B. - I.P.N. México, 17, D. F. MEXICO.

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Sectioning of both abdominal vagi, coeliac genglia, and all visible hepatic nerves, elicited quasi-aphagia in 4 rabbits (food-intake dropped from 100-150g/day to 0-25g/day); 2 of these were killed after 4 and 7 days, the other 2 died after 6 and 13 days. Another two rabbits exhibited aphagia for 2 and 3 days, followed by a prolonged strong anorexia (less than 60g/day) lasting 10 and 20 days; even after a month they had not reached the preoperative levels. Sectioning of both vagi alone produced one day of aphagia followed by a rapid recovery, attaining preoperative intakes after 3 to 6 days (4 rabbits). The same was observed after coeliacotomy alone (2 rabbits). The results suggest that hepatic deafferen tation, which would suppress information from the hepatic "gluco-ammonium-receptors" previously described, was the cause of marked and prolonged feding deficits, as efferent deficiences caused by vagotomy would be attenuated by coeliacotomy and viceversa. They also suggest that afferents in either of these nerve pathways are enough to compensate for the lack of the other one, preserving normal feeding, so aphagia would ensue only after complete liver denervation. (The author is a fellow of the SEDICT-COFAA).

EFFERENT INNERVATION OF A MECHANORECEPTOR. I.J. Russell and B.L. Roberts. The Marine Laboratory, Plymouth, England.

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Hair cells of the acoustico-lateralis system, including those of lateral-line organs, receive efferent innervation, the role of which is uncertain. Body lateral-line receptors of dopfish (Scyliorhinus) are innervated by efferent cell bodies in the medulla; impulses from these cells were recorded from filaments of the posterior lateral-line nerve. The efferent neurons are inactive in stationary fish and, in contrast with the efferent system of the cochlea, they are not directly excited by stimulation of the hair cells which they innervate. Effective stimuli are those which cruse the animal to move; for example, vestibular excitation, noxious chemical stimuli, and touch. Body movements, either spontaneous or provoked, are preceded by efferent activity which continues for the duration of the movement. When the fish is swimming steadily, the efferent system discharges rhythmical bursts at the swimming frequency, but not when body proprioceptors are excited by applying undulatory movements to the fish. Electrical stimulation of efferent fibres suppresses spontaneous afferent impulses. As in the case of the olivo-cochlear bundle, the inhibition produced is weak and short-lasting.

FONDEMENTS ET PREMIERS RESULTATS D'UNE NOUVELLE PREPARATION POUR L'ETUDE DIRECTE IN SITU DU COEUR DE MAMMIFERE : LA THORACOTOMIE GAUCHE DU LAPIN.

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Le lapin présente un médiastin complet ce qui, en pratiquant la thoracotomie gauche, autorise l'accès direct au coeur alimenté par le propre sang de l'animal oxygéné sans assistance ventilatoire par le poumon résiduel droit. Grâce à cette nouvelle approche peropératoire élaborée depuis 1964 il a été possible : 1°) de fonder la photométrie intravasculaire directe, 2°) de mesurer en continu à l'aide d'électrodes originales miniatures l'état d'oxygénation en valeur absolue des parois ventriculaires, ce qui renouvelle l'étude de la circulation coronaire, 3°) de mettre en évidence, par voie optique, une réaction polyphasique intracellulaire d'oxydo-réduction - un réflexe moléculaire -, 4°) de révéler une modification réversible du potentiel d'action monophasique épicardique in situ au cours du réflexe moléculaire cité qui est associé à des altérations importantes de la tension artérielle et de la pO2, et qui sont les conséquences notamment de l'administration transitoire par voie nasale ou sous-laryngée de CO2 ou de l'injection intraveineuse d'adrénaline. Cette préparation présente ainsi de nombreux avantages sur la préparation coeur-poumon de Starling.

STUDIES ON THE BIOCHEMISTRY AND ANTIGENICITY OF SPUTUM. 1444 Dept. of Internal Med., Nagoya Univ. KAZUO RYUGE and TATSUO SATAKE Sch. of Med., Nagoya, Japan.

Sputum is a hallmark of many respiratory diseases, but its identity has long remained to be clarified. This study was focused on its chemical composition and antigenic properties: Acid mucopolysaccharide was extracted from sputum as much as 0.40~4.80 mg/ml, and was found to mainly contain hyaluronic acid (70% hyaluronic acid, 20% chondroitin sulfate, 10% heparin). On the contrary, the acid mucopolysaccharide of the trachea mainly consisted of chondroitin sulfate. Secondly, to study antigenic properties of sputum, anti-sputum serum was prepared in rabbits by subcutaneous sputum injection. In addition, we tried to form antibodies by intratracheal sputum injection in rabbits, and succeeded to obtain anti-sputum serum. Sputum produced many lines of precipitation against anti-sputum serum in immunoelectrophoretic analysis. By previous absorption of the anti-sputum serum with normal human serum, three or four lines of precipitation were still obtained against sputum. They were possibly of lactoferrin, α_1 and β_2 mucogloblin. Sputum could be a potential factor in proggression of bronchial diseases.

TRANSPORT OF CALCIUM IN ISOLATED SARCOPLASMIC RETICULUM AS AFFECTED BY PROSTAGLANDINS, NOREPINEPHRINE AND 3'-5' ADENOSINE MONOPHOSPHATE. Sandra Sabatini-Smith. Dept. of 1445 Pharmacol., Univ. of Texas Med. Sch. at San Antonio, San Antonio, Texas, USA.

The present study was designed to study the effects of prostaglandins E_1 and $F_{2\alpha}$ (1 μ gm/ml), norepinephrine (5 x 10⁻⁶M) and 3'-5' AMP (1 μ gm/ml) on calcium (Ca) transport in stimulated and unstimulated preparations of cardiac sarcoplasmic reticulum (SR). from rabbit ventricles was isolated on a sucrose density gradient (0.3 - 1.0M) at 0°C in the presence of 5mM sodium azide. Electrodes cut from 45 mesh platinum wire cloth were placed on either side of a 0.45 μ pore diameter Millipore filter. Ca uptake by the SR (0.1 mgm protein/ml) was measured over a 10 min. period. Efflux was determined in the presence and absence of a 10 sec electrical stimulus. PGE $_1$ and PGF $_{2\alpha}$ significantly increased Ca uptake, 0.927 \pm 0.004 (\pm S.E.) and 0.968 \pm 0.010 μ mol Ca/mgm protein respectively (P<0.01). Incubation with NE and 3'-5' AMP did not differ significantly from control. Efflux of Ca was enhanced in the presence of the prostaglandins; NE had no effect either in the stimulated or unstimulated preparation. The inhibition of Ca uptake and efflux produced by 1 x 10^{-4}M lanthanum chloride was completely overcome by the prostaglandins in contrast to the lack of effect by NE and 3'-5' AMP.

INTRACELLULAR PH IN RELATION TO THE ARTERIAL CO2 TENSION.

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The intracellular pH of red blood cells (RBC), muscle (M) and mean
whole bedry (MWB), was determined in enotype to the DW The intracellular pH of red blood cells (RBC), muscle (M) and mean whole body (MWB) was determined in anesthetized dogs by means of the DMO method of WADDELL and BUTLER covering a wide range of arterial CO2 tensions. Regression equations were obtained relating pHi either to log pCO2 or to arterial pH. For an arterial pCO2 of 40 torr the following values of pHi were obtained: 7.20 (RBC), 6.93 (M), and 6.96 (MWB). For an arterial pH of 7.40 the corresponding values of pHi were: 7.28 (RBC), 7.00 (M), and 7.01 (MWB). The relation between the intracellular and the extracellular pH were pHi=0.92 pHa + 0.475 for the RBC and pHi=0.73 pHa + 1.579 for the muscle. It is concluded that the buffering power of the muscle cell exceeds the buffering power of the RBC. Mean whole body intracellular pH chiefly reflects the pH of the muscular compartment. Intracellular CO2 concentrations calculated from the DMO data of RBC and muscle agreed CO2 concentrations calculated from the DMO data of RBC and muscle agreed well with direct CO2 determinations reported in the literature.

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